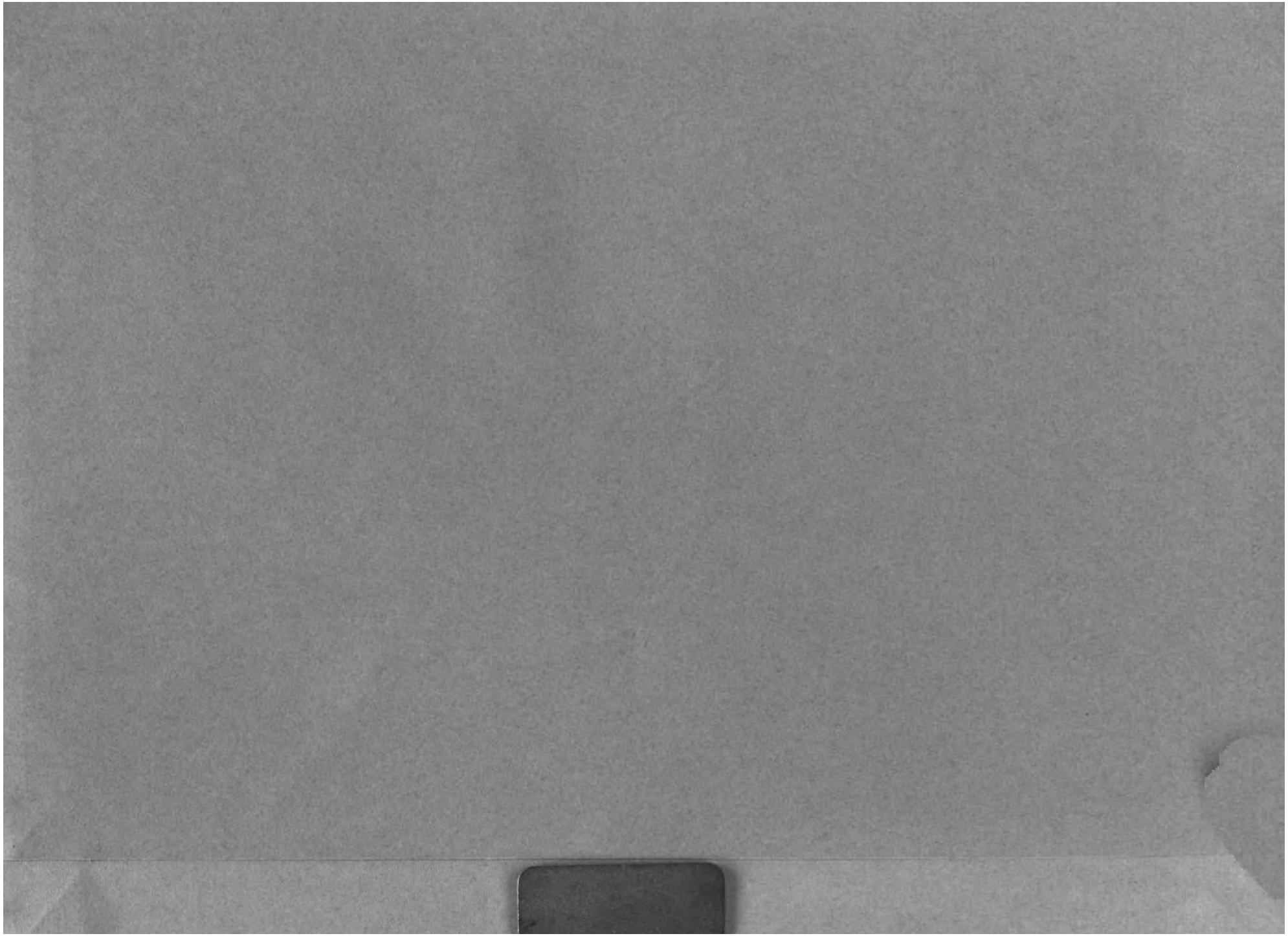

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AUTO-INOCULATION VERSUS HETERO-INOCULATION* IN THE TREATMENT OF ESTABLISHED INFECTION.†

By Dr. E. C. HORT.

IT is generally considered that production and maintenance of immunity to infection are questions only of protection against bacteria and other products.

The object of this paper is to submit, in the light of increasing knowledge of the phenomena of cellular pathology:

(1) That this interpretation ignores such additional factors in the sum-total of infection as autolysis and other anomalies of cell-metabolism, as well as the toxic products of such anomalies, and is therefore far too limited.

(2) That its acceptance accounts for the limited success that has so far attended all hetero-inoculative methods of fighting infective disease.

(3) That until this be realised no great advance is possible in the specific treatment, not only of conditions admittedly the result of bacterial invasion, but of many other diseases in no way related thereto.

In order to maintain such propositions as these I shall bring evidence to show:

(1) That spontaneous auto-inoculation, being a process of natural cure of infection by auto-serum and auto-vaccine therapy, incites the restraint of all the factors concerned; and—

(2) That artificial auto-inoculation is on that account immeasurably superior to hetero-inoculation, whenever it can be conveniently applied.

* The word "hetero-inoculation" is one that I have coined, from obvious analogies, to denote inoculation of immune serums, and of tuberculin and other vaccines from without.

† Delivered in part before the Royal Society of Medicine.

I shall also call attention to a novel method of interpreting temperature charts in terms of immunity curves, and shall refer to the advantages of measuring the anti-tryptic powers of the blood.

The Relation of Treatment by Inoculation to other Methods of Treatment of Established Infection.

There are three known methods of treatment of established infective disease: the general, the specific, and the surgical.

(1) Surgical treatment in its strictest sense aims at direct removal or destruction of the infective agent, or where this is not possible, at rendering such agent inoperable. There are two methods available—the mechanical and the chemical. The mechanical method is to remove the source of infection by incision and subsequent evacuation. The purely chemical method lies in the use of artificial antiseptics, whereby the infective agent is destroyed, or its action inhibited. The uses, abuses, and limitations of both methods need no notice here, though in passing it may be observed that a patient's own serum is often a better antiseptic than any the chemist can provide.

(2) General treatment of established infection aims, in common parlance, at building up the powers of reaction. In technical language its goal is efficient exhibition by the economy of effective response to natural or artificial stimulus; in other words, it strives to render specific treatment more effective than it otherwise could possibly be. Whatever methods, or combination of methods, of general treatment are adopted, climate, open-air *régime*, sanatorium supervision, diet, drugs, etc., are accessories only to specific treatment. They are, however, accessories that can never be dispensed with, whatever the advances made in specific treatment, because the latter is worse than useless unless the impaired power of reaction, which is the ultimate cause of successful infection, is capable of reinforcement by intelligently applied general treatment.

(3) Specific treatment of established infection may be defined as a direct bio-chemical attempt to repair the breakdown in the mechanism of immunity which has rendered the continuance of infection possible. Such attempt may be a natural effort on the part of the economy, or may be the outcome of artificial measures deliberately applied.

Natural specific efforts at immunity restoration are themselves the result of a natural process of spontaneous auto-inoculation, which may come into action immediately infection has become established, or from inflammation, or from the operation of various natural functions which no amount of rest can control.

So long as free communication between the lymph-stream and the focus of infection is maintained, spontaneous auto-inoculation is followed by simultaneously acting processes of active and passive immunisation.

Passive immunisation appears to be a process of automatic neutralisation in infective material by such antagonising substances as exist performed in a patient's own lymph and tissue-cells. Such process is, however, strictly limited; for not only in a given infection has the natural supply of pre-formed protective bodies already been drawn upon to allow of infection, but the balance has been gradually shrinking under the stress of its continuance. Hence, unless some provision be made for replenishing the original deposit, such balance sooner or later must become exhausted. This provision the economy ensures by a process of active immunisation.

Active immunisation may be defined as a process of stimulation of a patient's own powers of defence by and against such of his own tissue-cells and their products and such bacteria and their products as are for the time being his pathogenic guests. The expression of achievement is the manufacture of a larger supply of protective bodies, endowed with trophic functions, than before infection existed. The infective agent is, in fact, induced to forge an instrument for its own destruction from material supplied by the responsiveness of its host.

The process of active immunisation that immediately follows spontaneous auto-inoculation must not be confused with the natural but not spontaneous process that follows auto-inoculation induced by inflammatory hyperæmia. Further, it must be distinguished from the natural process of immunisation following intermittent auto-inoculation occurring in chronic diseases in which the focus of infection is from time to time insulated from the general lymph-stream. In the early stages of any infection, so long as free communication is maintained, the immediate operation of

active and passive immunisation may be sufficient to bring the infection to an end, provided that the economy is able to provide material for such immunisation.

Inflammatory hyperæmia.—Where, however, free communication is limited, or where, even with free communication, the pre-formed supply of antagonising substances is insufficient, or where, as a result of inadequate stimulus, response is weak, some further impetus to immunisation efforts is needed. This need the economy attempts to meet by inducing the form of hyperæmia known as inflammation. Inflammation we now know to be, within certain limits, a protective mechanism, one of the chief virtues of which lies in its increased determination of fertilising and restraining lymph to an infected area. In this determination a fresh supply of pre-formed bodies is provided, as well as fresh opportunity for the formation of new ones; in other words fresh processes of active and passive immunisation are set in motion. Inflammation *quâ* bacterial invasion is, therefore, actually a process of auto-serum and auto-vaccine therapy, especially provided by Nature to enable the economy to deal with an infection that has succeeded in gaining a footing. Inflammation is, in fact, the predominant factor in the economy's fight against infective disease.

Non-inflammatory hyperæmia.—In many cases, as for instance in apyrexial cases of chronic pulmonary tuberculosis and in many cutaneous and other lesions, free communication between the focus of disease and the general lymph-stream is interrupted. In such event the local supply of pre-formed antagonising bodies may be seriously curtailed. As a further result of this condition of relative insulation, itself often the result of inflammation, the stimulus necessary for the production of new anti-bodies is wanting. In order to meet this want, a condition of hyperæmia is intermittently induced by various natural agents, of which, for instance, the act of coughing is an excellent example. Cough is up to a certain point undoubtedly, in apyrexial cases, a conservative function, though liable to serious natural abuse. The condition of pulmonary hyperæmia that it produces is eminently favourable to the induction of processes of active and passive immunisation by means of natural auto-inoculations. There can be no doubt that such operation is frequently demonstrable, and it affords a good example of attempts made by Nature to overcome an infection that resisted its earlier and simpler methods. This consideration is in no way affected by the harmful effects of hyper-auto-inoculation so frequently observed after excessive cough or other quasi-involuntary movement, especially in cases accompanied by fever.

Artificial methods of immunity restoration.—The chief value of a study of natural methods of treatment of established infections lies in the clear idea that may be gained therefrom of the *rationale* of artificial measures. The chief of these are:

(1) Artificial auto-inoculation.

(2) Hetero-inoculation of immune serums as serums.

(3) Hetero-inoculation of vaccines.

(4) Local use of normal serums.

In all of these methods the same principles that guide natural methods of treatment are involved, excepting however, as will be seen, that these principles are in the case of artificial treatment infinitely more restricted in their application.

In the case of artificial auto-inoculation processes of active and passive immunisation are employed, *viâ* the various channels of artificial hyperæmia.

In inoculation of immune serums as serums a process of passive immunisation is alone employed, dependent, however, for its value on active incitation of immune body production in the animal employed.

Inoculations of immune serums as vaccines is said (1) to be often unwittingly employed, though never, presumably, with deliberate intent. The possibility of unconscious employment of immune serum as vaccine is supposed, though on insufficient grounds, to explain the excellent results obtained by the use of Professor Chantemesse's serum in enteric fever. There is, no doubt, much to be said for such a view, though a simpler and more satisfactory explanation is more probable.

Inoculation by vaccines is primarily a process of active immunisation, though once a definite increase of newly formed substances has been obtained, a process of passive immunisation must, provided intercommunication be free, also come into action.

The local use of normal serums is mainly a question of passive transference of pre-formed bodies to the site of damaged immunity, as I have

shown in the treatment of ulcerative conditions of mucous membranes and skin (2). It is not, of course, the ideal way of treating a local loss of cell-immunity. Its chief value lies in its approximation to the normal method by which the economy locally immunises itself, and is only to be exhibited when such natural methods cannot be conveniently set in motion.

THE PRESENT POSITION OF HETERO-INOCULATION.

The *rationale* of the practice of inoculation of immune serums and artificial vaccines has, of course, only one basis, involving as it does the exhibition of anti-bodies in response to very similar stimuli. The stimulus, in fact, is always from vaccines, whatever the source of such.

With regard to antitoxic serums the only one of pre-eminent value in treating infections already established is the diphtheria antitoxic serum. The worth of this serum, however, lies far more in indirectly protecting from toxins cells still undamaged than in direct restoration of integrity to cells already affected.

The value of all the anti-microbic serums, as at present employed, is, with one or two exceptions, admittedly small.

From time to time many suggestions have been advanced to account for this limitation. Some such suggestions are undoubtedly sound, such as exhaustion of complement, the co-existence of other organisms causing a mixed infection, and variations in the strain and virulence of the same organism. To these may be added the unquestionable absence from most of the anti-microbic serums of sufficient quantum of antitoxin. Even, however, when these suggestions have taken practical shape the results have not been strikingly improved.

With regard to artificially prepared bacterial vaccines, their possibilities have been widely exploited of late, and are still extensively proclaimed. That bacterial vaccine therapy has achieved a great deal, and will undoubtedly achieve more, it would be idle to deny. For many brilliant successes, mainly, however, in chronic and relatively unimportant conditions, have been recorded, as well as some in more serious diseases. Though the number of failures recorded is small, few will deny that the number of cases in which, even under ideal conditions, no benefit whatever has accrued, is very large. It is, in fact, worth inquiring if the movement is not leading us too far. For instance, to attempt to show, as has been attempted, that bacterial invasion is responsible for such conditions as diabetes, jaundice, pancreatitis, etc., and that these might therefore prove amenable to bacterial vaccines (4), is surely to lose a proper sense of perspective.

As in immune serum therapy so in vaccine therapy, many suggestions have been advanced to account for the limited success met with, such as the co-existence of mixed infection, variations in the strain of the particular organism concerned, and so forth. But here again the practical results of acting on these suggestions have too often been most disappointing.

If this presentment of the actual achievements of serums and vaccines be accurate, does it not seem as if some vital factor in the sum-total of infection, and of the means that should be adopted to antagonise such, has been overlooked?

That such is actually the case I shall now attempt to show.

The basis of all hetero-inoculative treatment is the familiar sequence of inoculation, intoxication, response. Response is at present only expressed in terms of specific anti-bodies to bacteria and their toxins, and the possibilities of cellulo-tropic response are ignored. It is generally held, in other words, that to protect a cell against parasitic invasion it is only necessary to provide against heterogenous agencies. Hence, a cell is not supposed to be in danger from autogenous factors either as the cause or the result of infection. It may be true that a healthy cell is not primarily in danger *de se*. There can, however, be no question but that disturbances of cell equilibrium, even when initiated from without, run a truly autogenous course. This being so they must be restrained by equally autogenetic means if integrity is to be directly maintained or restored. Integrity of form and function of a cell is, of course, constantly in jeopardy from the vicissitudes of cell-life. But a cell may be primarily attacked from within as well as from without. Its potential enemies from within are apparently not only its own intra-cellular enzymes, the very bodies essential to its life, but also the products of the morbid activity of such. Unless these are constantly restrained, equilibrium cannot be maintained. It is not the stomach only that can, under suitable

conditions, autolyse or digest itself; every tissue in the body has similar powers. That the body as a whole does not digest itself is apparently due to the inhibitory action of its anti-enzymes. These seem to be incited into being and action by the intra-cellular enzymes, on the strict analogy of toxin and anti-toxin. Between perfect integrity of a cell and the act of autolysis there are many grades of cell-aberration. Fatty degeneration, cloudy change, and many other processes, including possibly even cancer itself, are familiar examples. Between demonstrable auto-intoxication from the products of autolysis and other anomalies of enzymic activity and its earliest stages there must also be an infinite number of grades.

Under the stress of life there could be no escape from one or other of these aberrations unless there were some restraining influence constantly at work to hold a tendency to perverted action in check. This restraining influence may be defined as the protective response called out by cellular enzymes and their products whenever cell integrity is threatened by anomalies of cell-function. In the evolution of cell-maintenance, it is only this power of restraint that enables a cell not only to remain a cell of its own kind, but to remain a cell at all. In other words, natural selection transforms what was, in the first instance, accidental into protective purpose. To paraphrase Herbert Spencer, cell-life is the equation of cell-reaction. But the conception of reaction must not be confined to reaction against outside forces. It must also embrace a cell's reaction against its own enzymes, and against the products of enzymic activity. The very weapons with which a cell can destroy itself incite the restraint necessary to avert such disaster. When, therefore, a cell is damaged by bacteria or their toxins, its powers of restraint of what are then abnormal enzymic metabolic processes are impaired. It can of its own accord only return to a normal state by inciting responsive reaction in the fertilising lymph that supplies it. The sign of restoration is the exhibition of appropriate restraining bodies. Cell-life is, in fact, inconceivable in the absence of such restraint, which is the only intelligible explanation of the horror autotoxicus postulated by Ehrlich.

Hence, bacterially infected tissues must, I maintain, defend themselves, not against one factor only, bacteria and their products, but against three. The remaining factors are their own enzymes, and the products of their own enzyme activity. If attack is triple, defence must be triple. Antitoxin production *quâ* bacteria will do much, only, however, by protecting from harm cells still undamaged. It cannot directly enable cells already damaged to restore the condition of immunity on which effective cell-life depends. Many cells, no doubt, are injured beyond repair, but there must be also hosts of cells not beyond hope of spontaneously or artificially induced recovery. For such as these no antitoxin, bactericidal body, nor opsonin can be of the slightest avail, except by preventing further injury. If this be so, artificial specific treatment, which aims at production of bacterio-tropic bodies only to the exclusion of cellulo-tropic, can never meet with full success, so long as tissue damage is extensive. Further, the economy itself can never be relied on to spontaneously effect a cure unless it can consider the cellular element as well as the bacterial. The very fact that more people get well of infection than die of infection is strong proof that auto-cellulo-tropic restraint does actually and naturally occur, and is also the strongest possible argument for artificially inducing such restraint when natural efforts fail.

If the exponents of the hetero-inoculative method had not confined themselves to the use of vaccines of bacterial origin, and of artificial immune serums, dependent for their value on the production of bodies inhibitory to bacteria and their toxins only, there would have been the less excuse for this communication. Inasmuch, however, as the value of artificial vaccines made from emulsions of cells and cell-enzymes, and of immune serums dependent for their value on the production of bodies inhibitory to perverted enzymes and anomalies of cell metabolism, and to the products of such, has been neglected, the possibilities of such enlargement of the scope of hetero-inoculation are worth exploring. No doubt the inherent difficulties of preparing cell emulsions and enzymic vaccines are very great. There can, however, be little question that if they could be satisfactorily prepared, the addition of such to the armoury of the hetero-inoculator would enormously enhance the effect of his bacterial vaccines and serums. Even then, however, the combined value of artificial inoculation with cellular and bacterial vaccines would be considerably less than the same weapons when autogenously wielded,

as what I have to say on the subject of auto-inoculation is intended to show.

If these observations are well founded it is clear that future progress in immunity research is inseparably bound up with the study of cell enzymes. Such study must embrace the phenomena of autolysis and other anomalies of cell-metabolism, and their rotation to intra-cellular enzymes. Further, it must concern itself with intoxication from the by-products of morbid enzymic activity, and, above all, with the methods by which restraint of all these phenomena is naturally maintained.

Auto-Inoculation, Spontaneous and Artificial; its History, Value and Limitations.

I have now to show that the natural method of cure of infection is one of spontaneous auto-inoculation, and that it is therefore the best possible guide to artificial procedures when natural methods fail. I maintain, that is, that it is the best model, mainly because it antagonises all the factors in infection, namely, the tissue elements as well as the bacterial.

The following sketch, therefore, deals with an explanation of what is meant by the term "auto-inoculation." The history of the process is touched on, together with methods of induction and inhibition. Clinical estimation of induction and inhibition is then referred to, with illustrative charts. A few general considerations receive attention, and finally a comparison is made of the relative advantages of hetero- and auto-inoculation. Discussion of the best practical methods of artificially inducing auto-inoculation both in pyrexial and in apyrexial conditions is reserved for a future occasion, as also are clinical and hæmatological estimations of infective conditions in which fever is absent. Most of the charts referred to are from cases of pulmonary tuberculosis with fever. This disease has been chosen not only because it admirably illustrates the principles I desire to enunciate, but also because its frequency makes it particularly suitable for investigation.

Definition.—There seems to be some ambiguity as to what is meant by the term "auto-inoculation." The word "hetero-inoculation," with its familiar sequence of inoculation from an outside source, intoxication and response, is intelligible enough. The meaning of auto-inoculation is of course precisely similar if we allow for the prefix. The real ambiguity, therefore, is not as to what the word means, but as to how inoculation can be initiated from within. The difficulty at once disappears if we recognise that auto-inoculation can be produced spontaneously or artificially. Provided that there is free communication between an active focus of infection and the blood or lymph stream, natural or spontaneous auto-inoculation can clearly always be potentially in operation. Where, however, a focus is absolutely or relatively insulated, artificial means must be employed to induce hyperæmia, or, in other words, temporarily to destroy insulation. In the case of generalised infection, where, although inter-communication is free, response may be sluggish on account of stimulus being weak, artificial increase of stimulus has also to be employed. The effects produced by auto-inoculation are processes of active and passive immunisation.

History.—The history of the evolution of auto-inoculation as a therapeutic measure to be deliberately applied is intimately associated with that of hyperæmia, whether such hyperæmia be a natural phenomenon, as in inflammation and spontaneous inoculations, or artificially induced, as in any of Bier's methods. Inflammation, as we know, so long as it is neither inadequate nor excessive, is largely a protective and curative mechanism. The protection afforded thereby is partly due to transference of pre-formed tropic substances to a damaged area, and partly to the restraining response called out by stimuli from tissue cells and bacteria—in other words, to spontaneous auto-inoculations employed by Nature from the beginning of time, though unrecognised by us.

Artificial auto-inoculation has been unconsciously applied from time immemorial. Whenever fomentations, poultices, stupes, setons, blisters, and the like have been applied in the treatment of established infections of joints, skin, serous sacs, sense organs, abdominal or thoracic viscera, etc., our forefathers have unwittingly employed processes of active and passive immunisation by inducing a form of artificial hyperæmia. Such hyperæmia may be directly induced, or indirectly by the agency of neurons. This is also true of other methods of inducing artificial hyperæmia, whether arterial or venous. When, for instance, Ambroise Paré treated fractures with obstructive

bands, or when early Egyptian physicians employed light and heat baths, artificial auto-inoculations were in use. In 1894 the possibilities of active and passive hyperæmia were insisted on by Bier, whose methods have since invaded every domain of medicine and surgery. The conception did not, as is often supposed, originate with Bier (43). As pointed out by Adami (44), Bier's methods were based on the observations of Farre, Travers, Louis, and Frerichs. Even to-day, however, Bier does not seem to have fully realised on what a sound basis his work stands. He makes no mention of auto-inoculation, and yet it is to this factor as much as to any other that his happiest results are due. As an instance in point may be given the use of the mask in inducing hyperæmia in the treatment of apyrexial cases of pulmonary tuberculosis, a method which clearly foreshadowed the modern adoption of graduated labour in the treatment of that affection. The conscious and deliberate employment of the principles of auto-inoculation in the treatment of apyrexial cases of pulmonary tuberculosis will always be associated with the names of Freeman, Meakin (45), Wheeler, Paterson (46), and Inman (47). The remarkable results obtained by Paterson, and elucidated by Inman (48), in the use of graduated labour, are well known, though these authors have unnecessarily restricted their field to the treatment of apyrexial cases, as I shall presently show. This history of spontaneous auto-inoculation is of much greater antiquity, dating back as it does to the first invasion of man by infective disease. Whenever in man such disease has obtained a footing, and has run a chronic course extending into months and years, and whenever the subject of such disease has been cured or has progressed towards cure without the aid of outside specific treatment, spontaneous auto-inoculation has been in operation. Further, even when disaster has finally overtaken him as a result of any given infection, auto-inoculative efforts have at some stage or other in his disease been at work. Evidence in support of these statements will be produced later. In the meanwhile the following is worth consideration. It used to be said, on fairly sufficient grounds, that one seventh of the human race died of tuberculosis in some shape or form. In 1904 the Registrar-General informs us that 55,000 fatal cases of this disease were recorded in this country by him.

It was not long ago estimated in France that in that country one in three of the total population living to the age of thirty either had had, had then, or would have some form of tuberculous infection. In more recent days Hamburger, of Vienna, Ehrlich, von Behring, Naegeli, and others have estimated that by the time puberty is reached practically every European has received tuberculous infection demonstrable before or after death.

In this connection it may be said that the theory of universal infection is not, as at first sight appears, necessarily bound up with the doctrine of latent persistence of infection.

The proofs of statements as to fatality percentages are, of course, only approximately reliable. The more important proofs of statements as to the total incidence of a disease like tuberculosis must be largely inferential, though considerable evidence is available from post-mortem records of unexpectedly discovered tuberculous lesions.

The ratio of mortality to incidence in tuberculosis is of the highest importance, because if the theory of universal incidence be well founded, the wonder is not that in this country 55,000 die of the disease, but that such a huge majority get well. Since only a very small number of those that recover, or at least do not die of their infection, receive specific treatment by hetero-inoculation with tuberculin, it is clear that some other factor must have been at work to protect them. We have seen that no amount of general treatment is, in the absence of specific treatment (spontaneous or artificial), of the slightest avail in the treatment of a chronic disease like tuberculosis; hence such specific treatment can only have been supplied by unrecognised auto-inoculations.

If we turn to other infective diseases we find, for instance in 1904, that the ratio of deaths to notifications in London and the 256 towns was 63,052 : 9887 in the following affections: Smallpox, scarlet fever, typhus, erysipelas, enteric, continued relapsing fever, puerperal infection and diphtheria. The highest mortality was from diphtheria, 3726 with 27,748 notifications. The lowest, excluding typhus and relapsing fever, was smallpox, 329 with 5945 notifications. The other ratios of notifications to deaths were: Enteric, 11,210 : 1978; erysipelas, 17,100 : 727; typhus, 133 : 34; scarlet fever, 79,398 : 2414; relapsing fever, 184 : 21; and puerperal fever 1324 : 658.

Taken as a whole, the ratio of notified incidence to notified mortality was approximately in these diseases 10 : 1.

We know of no really efficient means of artificial specific treatment of any of these diseases except diphtheria. Hence the truth of the statement that in tuberculosis a much larger number of people recover from infection than die of infection is well supported by the analogy of the other infective diseases quoted.

The various methods of inducing and inhibiting auto-inoculation may be thus tabulated :

INDUCTION OF AUTO-INOCULATION.

(*A*) *Spontaneous.*	(*B*) *Artificial.*
(*a*) The occurrence of infection, given free communication.	All methods for inducing artificial hyperæmia, active and passive, such as—
(*b*) Inflammation.	(*a*) Counter-irritation.
(*c*) Involuntary movements, *e. g.* of heart, lungs, stomach, etc.	(*b*) All of Bier's appliances.
(*d*) All voluntary movements.	(*c*) Active and passive movements.
	(*d*) Light and heat.
	(*e*) Respiratory exercises.
	(*f*) Radium and X-rays.
	(*g*) High altitudes.

INHIBITION OF AUTO-INOCULATION (NATURAL AND ARTIFICIAL).

(*a*) Response called out by auto-inoculation in so far as it is expended on inhibiting activity of focus of infection.

(*b*) Removal or destruction of infective focus.

(*c*) Arrest of inflammation by cold, etc.

(*d*) Rest.

(*e*) Drugs : opium, belladonna, etc.

In this table the only points that can be noticed here are the inductive action of radium and X-rays, and the inhibitory action of rest and drugs.

As regards radium and X-rays, Neuberg (49) and Willcock (50) maintain that they have no restraining action on autolytic enzymes, though they are credited with inhibitory action on most other enzymes. Hence, according to Neuberg, cancer tissue exposed to radium undergoes autolysis much faster than cancer tissue not so exposed. Heile regards their action as due to liberation of leucocytic enzymes as a result of autolysis. The effect of both forms of emanation appears to be, in short, in the direction of direct or of indirect stimulation of action of autolytic enzymes. If this be so it becomes easily intelligible that radium should be a powerful weapon for producing auto-inoculation. For by undue activity of autolytic enzymes thereby incited not only will self-destruction of abnormal tissues be set up, but the stimulus afforded by abnormally acting enzymes may well be in itself a process of auto-induction leading to active immunisation against the aberration exhibited by cancerous cells. Experimental work in this direction is much wanted.

ARTIFICIAL INHIBITION OF AUTO-INTOXICATION.

The value of rest in inhibiting auto-inoculation is unquestionable. Rest, however, can never be absolute on account of the impossibility of controlling ordinary vital functions. At times, as shown by Dr. Arthur Latham (51), the immediate effect of complete rest on pyrexia, a failure of the temperature to rise sometimes indicating absence of auto-inoculative stimulus, is very striking. In other cases the effect is absolutely *nil* in this direction.

The number of drugs capable of controlling auto-inoculative processes is unfortunately limited. The only two drugs of general utility appear to be opium and belladonna. The effect of the administration of calcium salts in this direction is alleged to be due to their reputed power of retarding coagulation time *in vivo*. It is, in fact, widely believed that when given by the mouth calcium salts lead to increase of the calcium content in the blood, this to induction of acceleration of coagulation time of the blood, and this to inhibition of inoculation. Such accelerating action of coagulation time, however, has now been shown to be legendary, both by Dr. Golla (29) and T. Addis (52). The latter observer has shown from a long series of experiments that coagulation time is in fact unaffected by the oral administration of soluble calcium salts, and, be it noted, of citric acid. In order to test clinically whether calcium salts had any effect or not in inhibiting auto-inoculation, I undertook a series of experiments by administering by the mouth calcium lactate in half-drachm doses to cases of pulmonary tuberculosis with fever. The clinical test was to be an appreciable fall in a rising temperature after the exhibition of the drug. Reference to Chart T will show that in none of the eight observations was

the administration of the drug followed by any fall in temperature. In twenty-two other observations not charted, a fall of temperature within six hours of administration of the drug took place only twice. Obviously, therefore, the drug can neither be relied on to accelerate coagulation time *in vivo*, nor in any way to produce the definite clinical effects with which it has been credited.

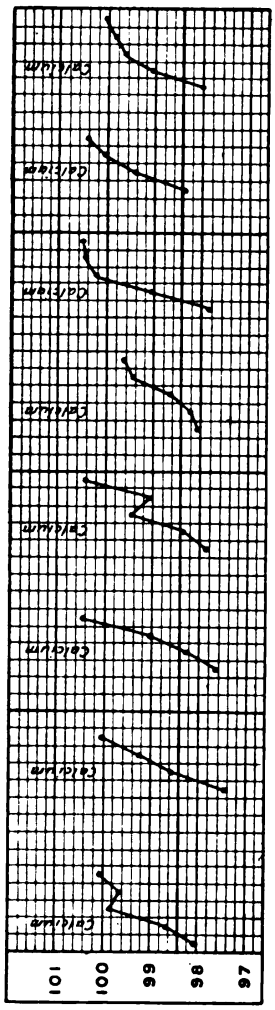


CHART T.—Four-hour chart showing non-effect on temperature of 30-grain doses of calcium lactate.

Spontaneous inhibition of auto-inoculation is effected by all those natural methods which the economy employs in order to arrest the disease.

METHODS OF ESTIMATING INDUCTION AND INHIBITION OF AUTO-INOCULATION.

(*a*) *Clinical Methods of Estimating Induction.*

In cases of infection accompanied by fever, it seems as if we have at hand a ready way of demonstrating not only the presence or absence of auto-inoculation, but also of presence or absence of response to such. The truth of the statement that a temperature chart can reveal the existence of intoxication and response is to some extent associated with the view that fever is a protective mechanism.

In the early days of medicine fever was undoubtedly held to be a conservative process. Subsequently the indiscriminate use of coal-tar products indicated the prevalence of an opposite teaching.

This has been again succeeded by the more rational view that within certain limits fever is essentially protective, and, in the case of infection of obvious source, actually an expression of effective neutralisation of such infection. In support of this view the following considerations are, amongst others, generally urged:

(1) Experimentally a high temperature enables animals to resist infection more readily than does a low, as shown by Richter after puncture of the corpus striatum.

(2) An animal like the fowl, normally resistant to anthrax, shows no such resistance if the temperature is artificially lowered, as was shown by Pasteur.

(3) In lobar pneumonia in man, apart from hyperpyrexia, the prognosis largely depends on the height of the temperature, as has been shown by Hale White and others.

(4) In broncho-pneumonia the same holds good, as was shown by Holt.

(5) It was shown in 1887, by Dr. C. J. B. Williams and Dr. C. T. Williams, that in pulmonary tuberculosis—

(*a*) In the so-called first stage 80 per cent. of cases either maintained or gained weight, in spite of, or, as I should prefer to say, perhaps even because of, fever. The number of cases was twenty-five.

(*b*) In the so-called second stage 5 per cent. gained weight. The number of cases was nine.

(*c*) In the so-called third stage 27 per cent. maintained or gained weight, whilst 72 per cent. lost weight. The number of cases was thirty-three.

So that of ninety-one cases, all febrile, in all stages, of whom more than one third were in the "third" stage, and therefore far less able to efficiently immunise themselves than cases in earlier stages, no less than 56 per cent. maintained or gained weight.

(6) High temperatures are fatal to many micro-organisms.

If it be true that reaction against infection can be expressed in terms of the increased work done by tissue cells, then we should expect to find a direct relation, within common-sense limits, between the amount of pyrexia and the degree of immunity production.

The possibility that temperature charts might prove to be of great service in estimating immunity response in bacterial infections was demonstrated by Dr. Arthur Latham (53) in 1908 in a most valuable contribution to the study of immunity delivered before this Society. His observations were based on the inverse ratio that he found to exist in many cases between the temperature and the opsonic index. If it be held that estimations of the latter, especially in tuberculosis, are, even if consistent, not a trustworthy gauge of immunity response as a whole, some other controlling standard must be substituted. This does not, however, in any degree detract from the value of his contention that in many cases it is possible more or less accurately to read an immunity curve in terms of a temperature chart. This contention, in spite of the fact that it is still unproven from blood examinations *quâ* opsonins or other immunising bodies, is, I submit, true, though, as I shall show, much more information can be gained from a study of temperature charts than has hitherto been elicited. Before proceeding with the evidence it is worth noticing the somewhat fallacious answer recently given to the suggestion that reliable information could be gleaned from the clinical charts as to immunity production. In dealing with the subject, Sir Almroth Wright (54) maintains that the temperature curve is a measure of intoxication but not of immunisation, and that there is no direct and constant relation between such curve and the production of anti-bacterial bodies. This statement is surely a confusion of terms. It has been well said by Pembrey that fever is not an entity, but a convenient clinical term for a group of phenomena with a more or less definite sequence and origin.

If this be so, a fever chart, if it means anything at all, ought to reflect such origin and sequence.

The factors in immunisation are stimulus, plus, where such be possible, response. In other words, the combination of stimulus and reply to stimulus represents what we call the act of immunisation, since active immunisation is obviously impossible without the impetus of intoxication. Hence if the temperature curve is also an immunity curve it must be a measure of intoxication and response. If there is no response, the temperature curve in a pyrexial case shows its absence as well as its presence, and is therefore a measure of absence of immunisation. Hence, there may be, I maintain, a most direct and constant relation between a temperature curve and the production of protective bodies. That such relation actually does exist in many cases is suggested, though by no means proved, by a study of the ensuing charts.

Charts 1–4 are of cases of pulmonary tuberculosis from various sources who did well under general treatment. No one of them received

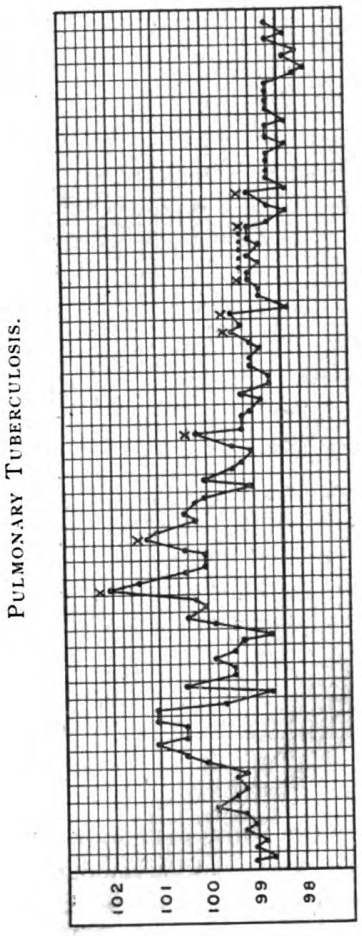


Chart 1.—Continuous evening chart.

artificial specific treatment of any kind. The charts are not, as they appear to be, ordinary charts showing diurnal variations of temperature. In each case they represent the evening temperature joined by a continuous line. The reason for this procedure is the great difficulty of getting a correct idea of the general course of intoxication and of response from a series of sheets recording diurnal variations. It is,

in fact, impossible for the eye to receive an exact impression of a chart as a whole, if in a disease such as tuberculosis, with wide excursions between morning and evening, the ordinary charts are studied. The abbreviated method has the additional advantage of reducing to small compass the readings of many weeks. Each chart given below is capable of registering the observations of four months. In order to make clear the object of recording in a graphic manner what I conceive to be effective response to spontaneous auto-inoculation, the broken curve of declining indices has marked on it at intervals the letter X. Whenever, therefore, this letter appears, it is intended to indicate

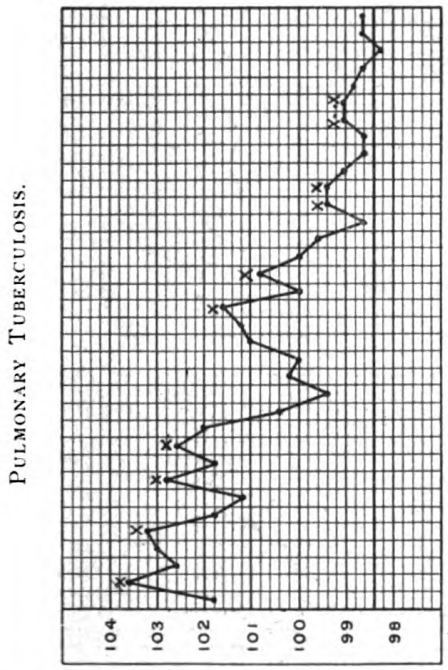


Chart 2.—Continuous evening chart.

the crests of the effective auto-inoculative wave. It will be noticed that each crest is, as a rule, lower than preceding crests, higher than succeeding crests, and is separated from its fellows by intervals of from one to fourteen days. The smaller waves noticeable in the charts are not lettered.

Chart 1 is from a case of pulmonary tuberculosis with well-marked signs in both lungs. The sputum contained tubercle bacilli. The total gain in weight during treatment was 19 lb. Improvement was progressive. The case is of interest, because not only does it show to perfection the broken curve of declining indices, but it also shows the absence of this curve in the first month of treatment before there was any sign of clinical improvement.

Chart 2 is from a case of pulmonary tuberculosis under treatment for five weeks only. The broken curve of declining indices coincided with well-marked clinical improvement.

Chart 3 is from a case of pulmonary tuberculosis published by Dr. F. W. Burton-Fanning, and treated by him in 1896 under the open-air *régime*. Tubercle bacilli were present. Fever declined, he said, after four months' treatment, and in a further

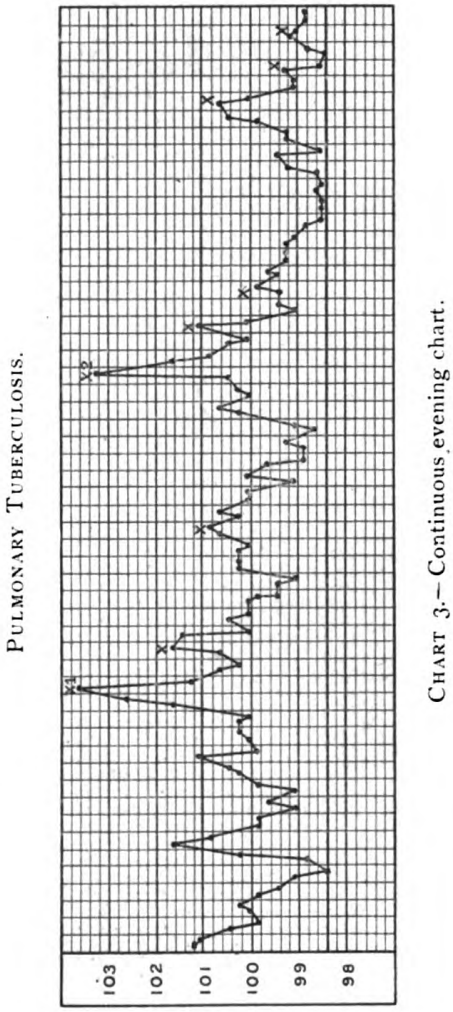


Chart 3.—Continuous evening chart.

seven months all physical signs and symptoms, as well as tubercle bacilli, had disappeared. The total gain in weight was almost 14 lb. He was well and at work twelve months after discharge. The case is interesting on account of the favourable course with many weeks' high fever. The chart shows very well, not only the broken curve of declining indices, but also the sharp elevations at X1 and X2, which seem to have been followed by great improvement.

Chart 4 is also one of pulmonary tuberculosis

published by Dr. Burton-Fanning. There was, he says, a large cavity in one lung and a softening deposit in the other. The duration of treatment was four months and the gain in weight 16 lb. Result —arrest and great improvement. The gap in the chart denotes the patient's temporary absence. On return she evinced a fresh rise from a spontaneous auto-inoculation, which was again followed by a further declining curve and final descent to nearly normal.

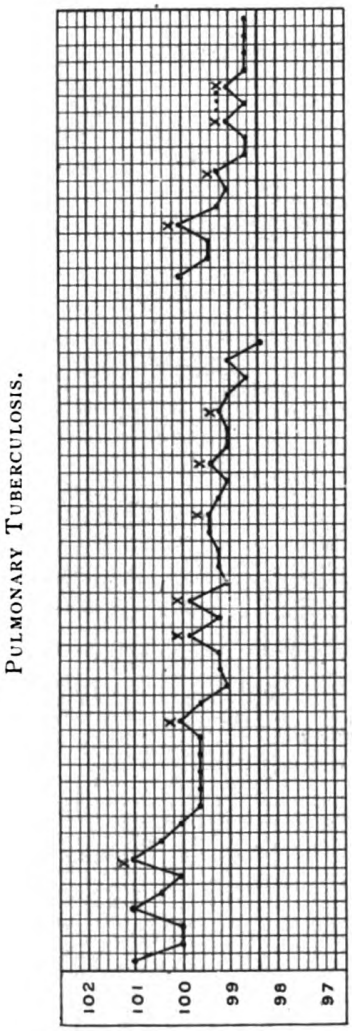


Chart 4.—Continuous evening chart.

Chart 5 is from a case in whom no attempt at inoculative treatment was attempted. He went steadily from bad to worse, and the chart shows almost total absence of attempts at effective response to spontaneous auto-inoculation. This chart is reproduced in order to demonstrate the reverse picture to that shown in Charts 1–4.

Charts 6–10 represent broken curves of declining indices in cases of enteric, scarlatina, influenza and non-tuberculous broncho-pneumonia. They are reproduced to show that the picture of spontaneous and effective auto-inoculation is not confined to

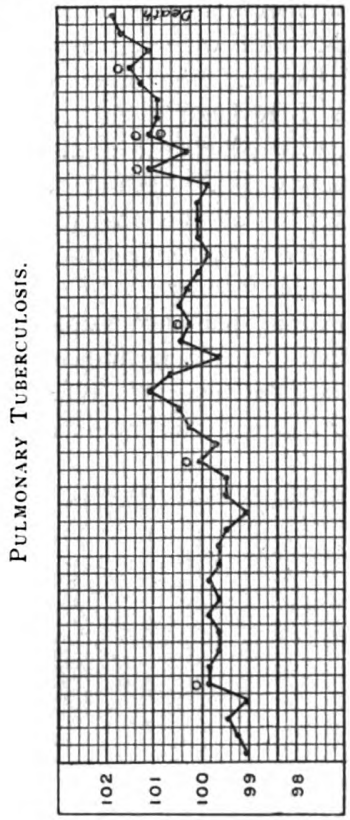


Chart 5.—Continuous evening chart.

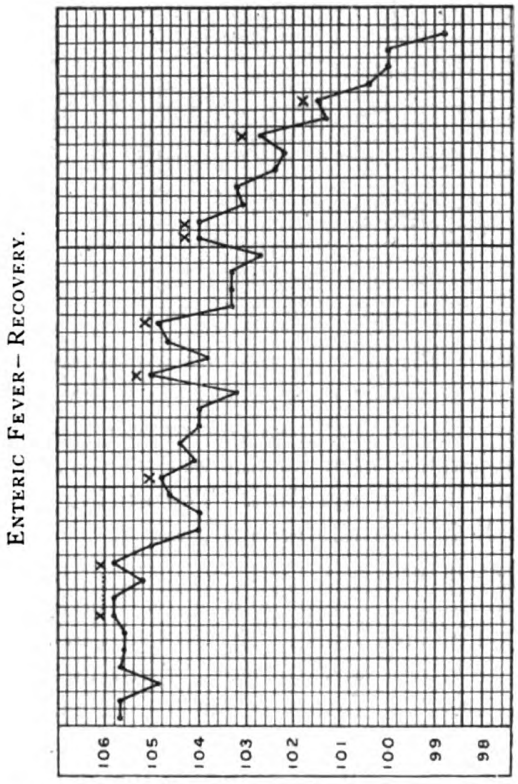


Chart 6.—Continuous evening chart.

tuberculosis. The two enteric charts are continuous evening temperatures, the morning temperatures being again omitted as obscuring the point at issue. The influenza chart is a four-hourly one. In acute infections running a short course, such as scarlatina, influenza and measles, the insertion of morning temperatures is essential to correct interpretation. Since the remittency is slight there is no difficulty in reading.

Scarlet Fever—Recovery.

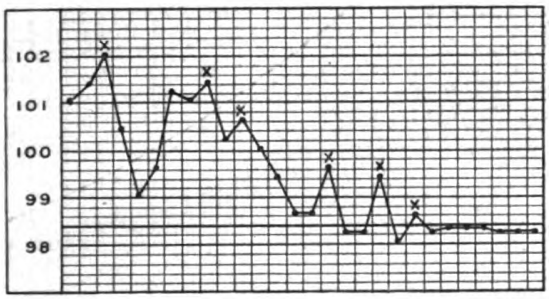
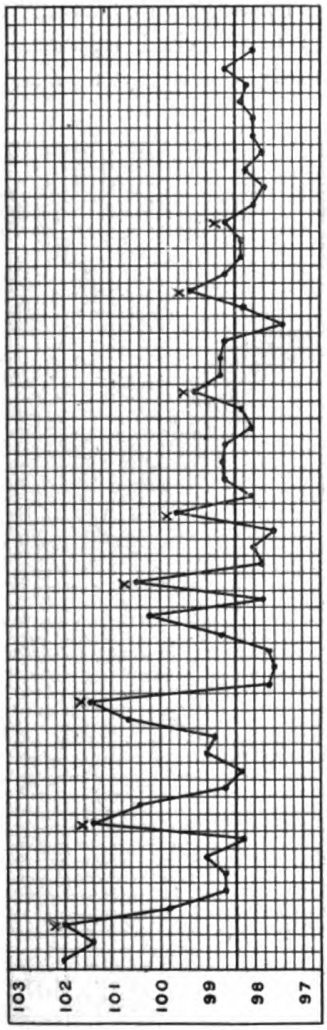


Chart 7.—Continuous evening chart.



Influenza—Recovery.

Chart 8.—Four-hourly.

Broncho-Pneumonia—Recovery.

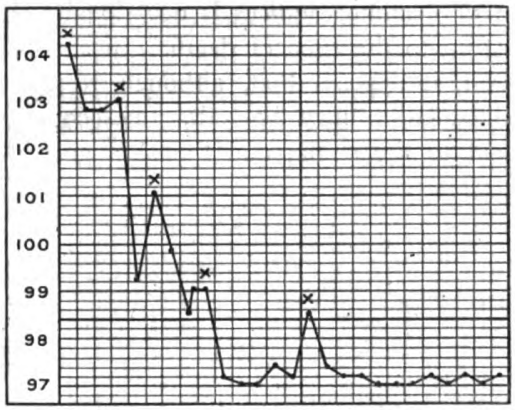
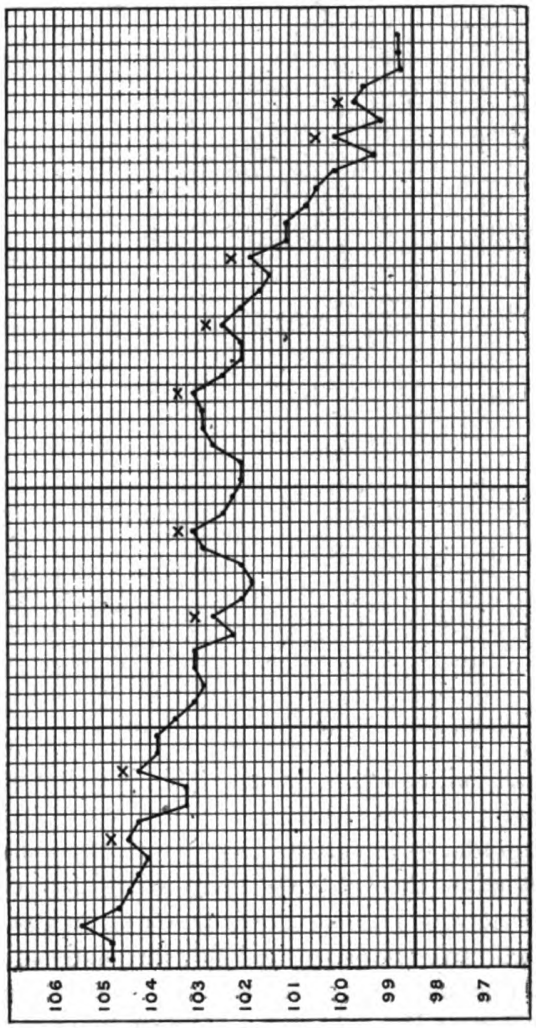


Chart 9.—Continuous evening chart.



Enteric Fever—Recovery.

Chart 10.—Continuous evening chart.

Chart 11 represents an exactly opposite type to that shown in Charts 6–10. Effective response to

auto-inoculative stimulus is, as a rule, conspicuously absent in cases in which death finally occurs.

This is a convenient place to notice that in some cases ultimately ending in death a broken curve of declining indices is occasionally shown almost up to the time of death. In such cases, however, it appears that, although response to auto-inoculation may be fair, the economy is unequal to the strain, and the ship goes down,

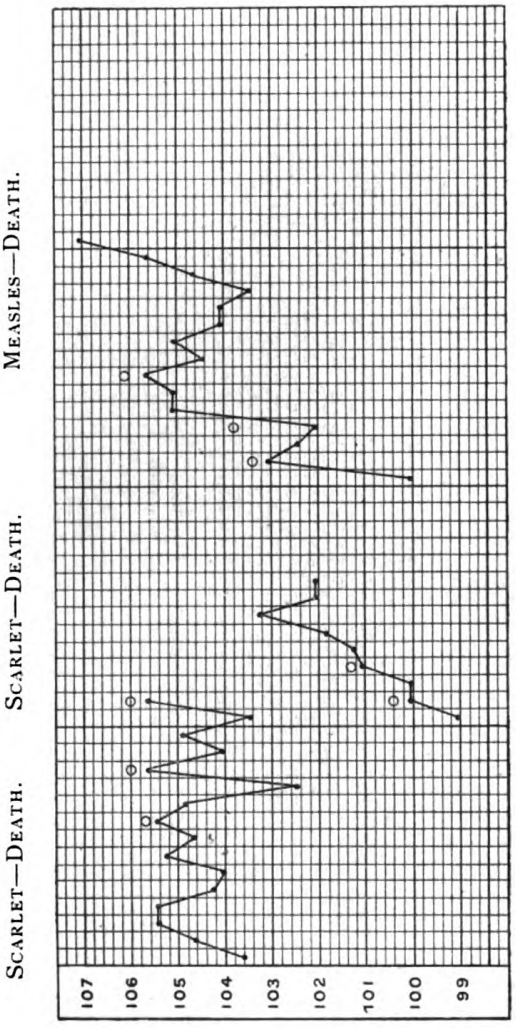


Chart 11.

literally with all flags flying. This is well seen in Chart 5.

In order to represent more graphically still the contention that a temperature chart may often indicate with great accuracy presence or absence of effective response to auto-inoculation, the following auto-inoculation curves are reproduced.

Chart 12 is moulded from temperature Chart 2, and will be found to represent with sufficient accuracy for practical purposes the rise and fall of intoxication and response, leaving out of account minor variations.

Pulmonary Tuberculosis.

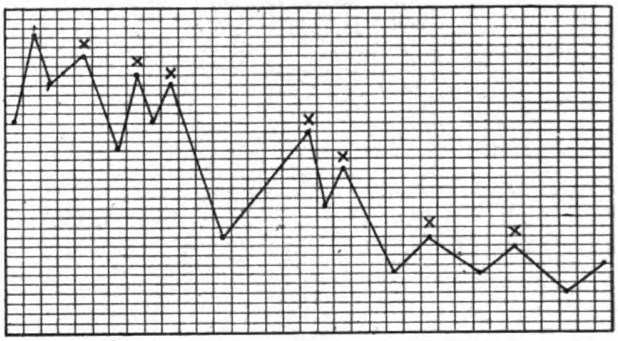


Chart 12.—Intoxication-response curve of case doing consistently well.

Chart 13 is moulded on Chart 1. While Chart 12 represents undisturbed response to effective auto-inoculations, Chart 13 represents an early

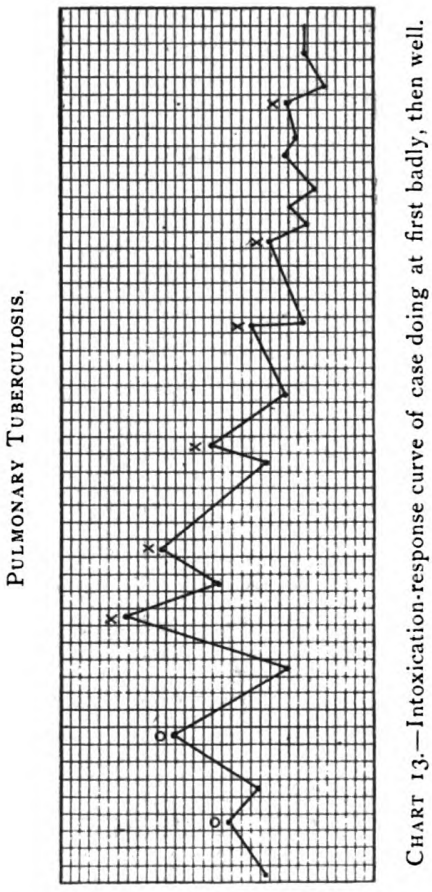
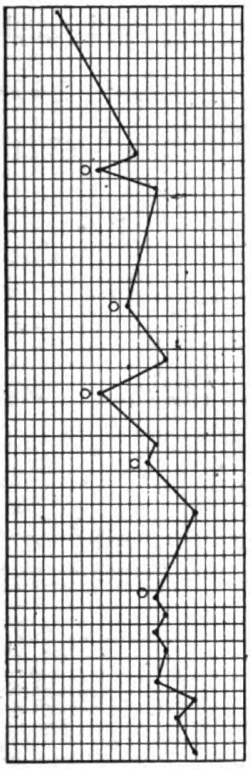


Chart 13.—Intoxication-response curve of case doing at first badly, then well.

stage of nearly four weeks' duration in which response to such was in abeyance, and in which the patient was actually losing ground.

Chart 14 represents in the first half a partial



PULMONARY TUBERCULOSIS.

CHART 14.—Intoxication-response curve of case doing badly. Death.

absence of response to auto-inoculation which was completely overpowered, and eventually, in the

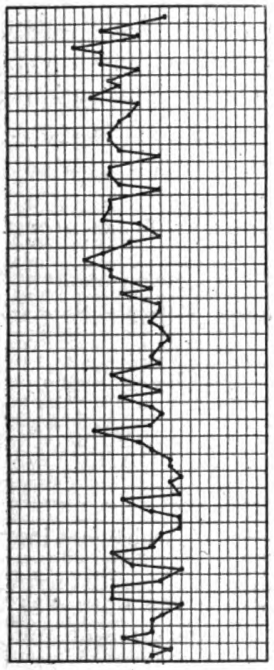


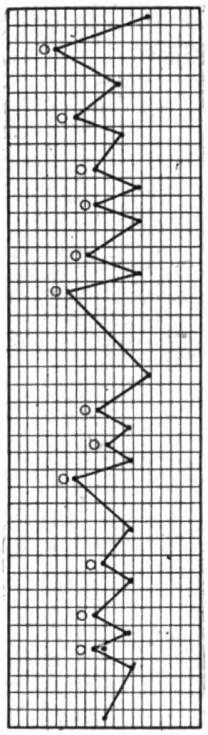
CHART 15.—Continuous evening chart.

second half, ended in death; the picture of Chart 14 is the inverse therefore of 12 and 13.

Chart 15 represents a case of pulmonary tuberculosis which, clinically, was not markedly going down hill, but in which no material improvement was taking place. Towards the end of the chart, however, a slight increase in the extent of lung involved is reflected in the chart.

Chart 16 represents the spontaneous inoculation curve moulded on Chart 15. It will be found to represent a striking contrast to Chart 13, in which the patient did very well, and to occupy an intermediate position between 13 and 14, Chart 14 being that of a case ending in death.

Having thus sketched the course taken in certain cases of pulmonary tuberculosis by the temperature



PULMONARY TUBERCULOSIS.

CHART 16.—Intoxication-response curve of case doing neither well nor ill.

charts and by what appear to be their intoxication-response curves where they were—

(*a*) Progressing towards cure;

(*b*) Rapidly going down hill;

(*c*) Doing neither well nor ill;

it remains to study the charts and auto-inoculation curves of cases in classes B and C in whom the course has been artificially altered by artificial means.

Charts 17–23.—Of these, 17, 20, 21, 22, and 23 are reproduced to demonstrate how far cases of pulmonary tuberculosis that are not doing well can be artificially induced to approximate to cases that are doing well. The procedure adopted in all

cases was one of artificial auto-inoculation, modelled on the information gleaned from Charts 1–17 of natural auto-inoculation. The material is not large, but it affords sufficient justification for extended trial of the method. In other cases not here reported in which tuberculin has been employed, the results obtained bear no comparison with the results obtained with artificial auto-inoculation, although the guiding principles were identically the same.

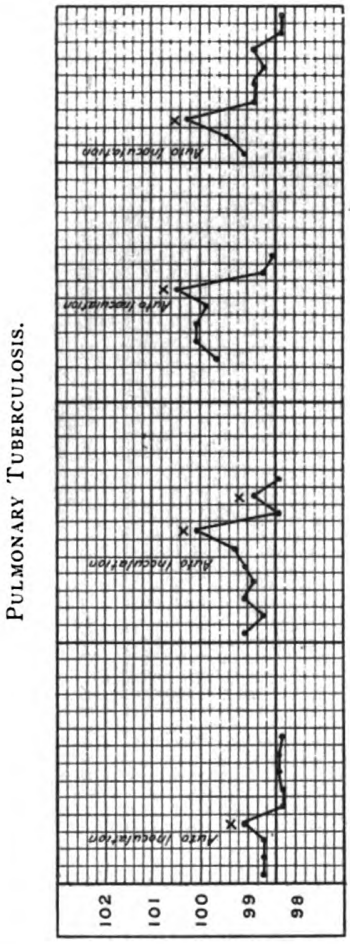


Chart 17.—Auto-inoculations. Correct dose.

Chart 17 represents four isolated phases where a correct auto-inoculative dose was given, as shown by the lower range of temperature following the apex of response preceding it. Such curves are apt to be misinterpreted as instances of hyper-inoculation. That such interpretation is erroneous, however, is shown by the coincidence of clinical improvement with the broken curve of declining indices. This consideration also applies to the injection or other administration of tuberculin.

Chart 18 represents three isolated phases of three different cases where the dose was actually excessive, as shown by declining physical improvement and absence of broken declining curve. It is therefore labelled a hyper-inoculation chart. This chart is a true intoxication record, with practically no evidence of response.

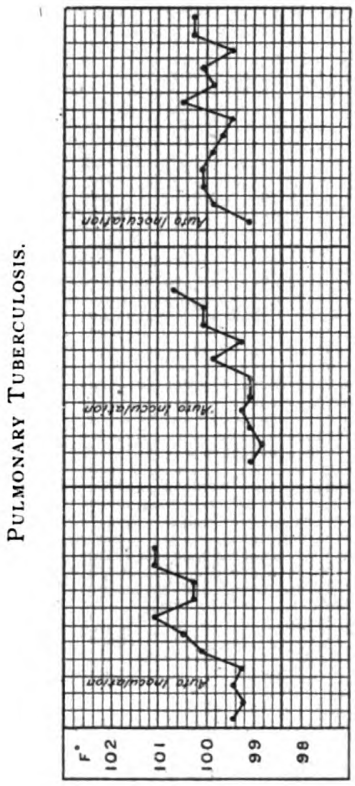


Chart 18.—Hyper-inoculation. Incorrect dose.

Chart 19 represents two isolated phases of two different cases where the dose was too small, as evidenced by practically no result following inoculation, either in the chart or in clinical signs. It is therefore labelled a hypo-inoculation chart.

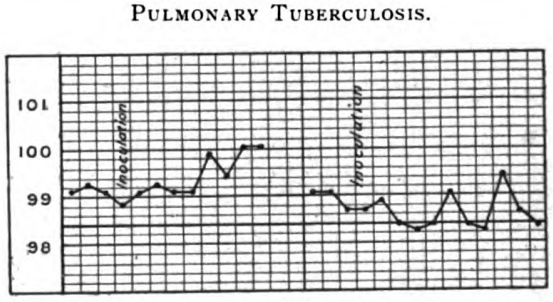


Chart 19.—Hypo-inoculation. Incorrect dose.

(*To be continued.*)

THE CLINICAL JOURNAL,

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SOME USEFUL PRESCRIPTIONS IN THE PRACTICE OF GYNÆCOLOGY.*

By VICTOR BONNEY, M.S., M.D., B.Sc.Lond., F.R.C.S.Eng., M.R.C.P.Lond.,

Assistant Obstetric Physician to the Middlesex Hospital; Surgeon to Out-patients to the Chelsea Hospital for Women.

MR. PRESIDENT and GENTLEMEN,—In dealing with a large number of women in the course of out-patient work at a gynæcological hospital or department, it is possible to divide them into two classes: (1) Those whose alleged symptoms are associated with physical signs of disease, and (2) those who present no physical signs in spite of alleged symptoms.

The treatment of the first class is chiefly surgical, or, if we include the use of the pessary, almost entirely mechanical. This is the best side of gynæcology, and places it in the position of an accurate science and almost purely surgical art. But, just as the surgeon practising branches of surgery other than gynæcology is called upon occasionally to administer drugs (either in place of, or more commonly as an adjuvant to, surgical measures), so a certain number of this first class of patients require medicinal treatment to effect or complete their cure.

The patients comprising the second class, to which I have drawn your attention, are those complaining of a whole host of aches, pains and feelings, which, in their irregular distribution, their evanescent or protean character, and their want of association with any physical signs capable of explaining them, present the most difficult problem in the whole range of gynæcology.

This class is treated chiefly by drugs, empirically administered, for in the absence of the physical signs of disease accurate diagnosis is impossible, and the

* Delivered before the Chelsea Clinical Society.

origin of the symptoms becomes entirely a matter of personal opinion. Owing to the peculiar temperament of gynæcological patients and the extraordinary degree to which a mental element complicates their pain sense; I think there is no specialty in which it is so important to abstain from dogmatic diagnosis, unless it can be founded on definite physical signs. Thus the statement that a patient is suffering from "ovaritis" simply because she complains of pain in the left side of the lower abdomen is unjustified, and the gynæcologist who dogmatically makes such diagnoses and treats cases with assurance on such assumptions is not much above the level of a quack, sincere in his belief though he may be.

I do not mean to suggest that a practitioner should not treat a patient unless some organic defect can be discovered on which to found a diagnosis. Such cases demand relief for their symptoms, real or imaginary, and have to be attended to, but it is well in dealing with them to realise the uncertain ground on which one stands, and to avoid unreasoned faith in personal powers of intuitive diagnosis.

Medicinal treatment, then, in gynæcology is rarely a method of precision, not because the physiological effects of the drugs are unknown, but because in the bulk of cases in which they are used the real nature and ultimate origin of the symptoms are hidden from us.

In the course of some years in an out-patient department at a women's hospital one picks up a good deal of knowledge of the use and value of drugs in women's complaints. This knowledge is quite empirical, and is often flatly opposed to orthodox or logical conclusions. One learns that in hospital pharmacopœiæ there are certain prescriptions which never do any good, no matter what they are prescribed for, logically or otherwise, whilst there are others which seem to give satisfaction to most patients, even though they be complaining of totally different symptoms.

To pass then from the general to the particular, I will proceed to say a few words about each of certain groups of drugs commonly used in the practice of gynæcology.

Drugs that Act Beneficially on Uterine Hæmorrhage.

Ergot.—Ergot is the only drug in the pharmacopœia of gynæcology of which the pharmaco-dynamics are accurately known, and the action of which may be termed specific. I usually give ergot in acid solution combined with strychnine, thus:

℞	Ext. ergot liq. . .	♏xxx
	Liq. strychnine . .	♏v
	Ac. hydrochlor. dil. .	♏x
	Aqua ad. . . .	℥j

I believe its action is more powerful when administered this way.

It is occasionally desirable to combine ergot with iron in the treatment of uterine hæmorrhage complicated with anæmia. The acid character of the mixture may be maintained, thus:

℞	Ext. ergot liq. . .	♏xxx
	Tr. ferri perchlor. .	♏v
	Ac. hydrochlor. dil. .	♏x
	Aqua ad. . . .	℥j

or if a less astringent form of iron is indicated the following prescription meets the case:

℞	Ext. ergot liq. . .	♏xxx
	Ferri tartras . .	gr. x
	Ac. tartaric . .	gr. x
	Aqua ad . . .	℥j

Strychnine may be added to either of these.

Personally I always give ergot in solution if possible, but it may be administered as ergotin. Some of the solid forms are quite inert, a failing which is likely to beset any which have been kept too long. Some ergotin pills, for instance, are probably passed *per anum* without change. The best preparations are those made by the larger druggists. Thus Burroughs, Wellcome & Co. put up a variety of tabloids containing ergotin in various combinations; these are excellent. I do not propose to discuss the hypodermic administration of the drug, which in ordinary gynæcological practice has no place.

Ergot is by far the most satisfactory of the purely gynæcological drugs. Its action in stopping uterine hæmorrhage is undoubted, but there are certain conditions in which its use is contra indicated. Especially so is this the case in *uterine fibroids*, except under unusual conditions. It has been shown that the continuous administration of ergot by producing an arterial contraction throws an increased strain on the cardiac muscle. This is the more harmful, because in these women considerable anæmia is present as well. Hence one finds, as Wilson pointed out, that old cases of

"fibroids" who have been treated for years by medicinal measures exhibit cardiac dilatation, which is a serious drawback to the usually inevitable operation. *Given a condition in which ergot, if prescribed, will have to be taken over a prolonged period and the use of the drug at all is contra-indicated.* There is only one proper treatment for uterine myomata—their removal—which should be carried out immediately they begin to give rise to symptoms. So much has the surgery of these tumours been improved that in competent hands and in early cases the risks of the operation are less than those of the removal of a chronically inflamed appendix.

There is another class of patient in which the use of ergot is contra-indicated, namely, in cases of incomplete abortion with a view to the expulsion of the retained fragments. It is true that it is not infrequently successful, but in the cases in which it fails—and they are the majority—it is responsible for much loss of time and the consequent increased risk of septic infection. The proper treatment for these cases is exploration of the uterus under an anæsthetic.

As a general rule ergot is likely to be successful in uterine hæmorrhage when the consistency of the organ is soft, whereas in cases where it feels hard and firm not much is to be expected. There is one conspicuous example of this in the condition known as chronic fibrotic metritis. Here, as the result of a chronic inflammatory process, the musculature becomes degenerate and there is a diffuse overgrowth of fibrous tissue, involving, in advanced cases, the whole thickness of the uterine wall. These cases present exceptionally severe menstrual hæmorrhage, which ergot entirely fails to control; the correct treatment is, therefore, hysterectomy.

Ergot, when used to lessen menstrual bleeding, should be given intermittently, beginning about two days before the onset of the period and continuing its exhibition so long as loss is going on, and for from two to seven days afterwards. In cases of subinvolution after labour and abortion, on the other hand, it should be taken continuously for several weeks, and the same rule applies to the convalescence after currettage or the removal of polyps and other conditions in which it has been necessary to forcibly dilate the cavity of a soft and bleeding uterus.

Before leaving ergot may I say a few words on an aspect of its use which has made it the most fatal drug in the whole materia medica. I refer to *its administration in cases of genital hæmorrhage without the precaution having previously been taken of making a digital examination to discover the cause.* You would be surprised what a number of cases of inoperable carcinoma of the cervix come before a gynæcologist with the history that though they had been treated with ergot for several months for the hæmorrhage of which they complained, no internal examination had even been suggested. The bleeding in these neglected cases is usually attributed to the "change of life." No more fatal mistake can be made than to suppose that the climacteric is normally associated with unusual loss of blood. It is not so. At that period more than any other an immediate examination as to the cause of any irregular hæmorrhage should be insisted on, and if refused the practitioner should decline to treat the case.

Hydrastis and hamamelis.—There are many other drugs which have been used either to replace ergot or assist its hæmostatic action.

Of these I will first mention hydrastis and hamamelis, which I usually use in combination thus:

℞	Ext. hamamelidis liq. .	♏xv
	Ext. hydrastis liq. .	♏xv
	Liq. strychniæ . .	♏v
	Ac. hydrochlor. dil. .	♏x
	Aqua ad . . .	℥j

or with the addition of ergot, thus:

℞	Ext. ergot liq. . .	♏xx
	Ext. hydrastis liq. . .	♏x
	Ext. hamamelis liq. .	♏x
	Liq. strychniæ . .	♏v
	Ac. hydrochlor. dil. .	♏x
	Aqua ad . . .	℥j

They certainly do sometimes succeed where ergot fails, and they do not cause the uterine contraction pain which ergot not infrequently produces when taken to check menstrual hæmorrhage. This pain or "stomach-ache," to use the women's expression, is sometimes so severe that I have known patients refuse to take the latter drug.

Instead of the liquid extract of hamamelis, hazeline (Burroughs Wellcome & Co.) may be administered in doses of one fluid drachm. It is probably the more active preparation of the two.

Hydrastinine.—The active principle of hydrastis I have used in one or other of the useful tabloid combinations with ergotin and other drugs, and with satisfactory results.

Cannabin tannate. — Of this derivative of cannabis indica my experience is limited to the tabloid preparations I have referred to. It may be given in doses up to four grains for menorrhagia.

Styptol and Stypticine.—These two drugs, the pthallate and hydrochloride of cotarnin respectively, I can speak favourably of. I have had most experience of the former, which I have used a good deal as an alternative to ergot in certain cases. The dose of either is half a grain. Styptol undoubtedly controls certain anomalous forms of uterine hæmorrhage, over which ergot has no effect. Beyond this, it has the power of alleviating certain forms of pelvic pain, chiefly those of menstrual incidence associated with an abnormal amount of loss. I prescribe it thus:

℞ Tablet Styptol (Knoll), mitte. tab. xxx

One tablet to be taken three times a day after meals.

From the point of view of hospital practice it has the disadvantage of being very expensive. At Chelsea we gave it in powder form for a while, but it tends to perish if prescribed in this manner.

Stypticin is present in some of the Burroughs Wellcome and Co. tabloid preparations I have referred to.

Bryony.—This drug is largely used, I believe, by homœopathists. It is supposed to check menstrual hæmorrhage, but is very little known in allopathic therapy. I must say I have found it a distinctly useful drug, not so much from the point of view of hæmostasis, but because in combination with aletris and other drugs it has a sedative action in certain varieties of pelvic pain. I have used it also in combination with ergot, hydrastis and other hæmostatic drugs.

℞	Tr. bryoniæ	♏x
	Potass. bromid. . . .	gr. xx
	Inf. cinchona ad . . .	℥j

t.d.s.; or

℞	Tr. bryoniæ	♏x
	Tr. hyoscyamii . . .	♏xxv
	Ext. viburnium prunifolium liq.	♏xxx
	Aqua camphoræ ad . .	℥j

represent two such prescriptions which have been used with occasional success.

Gossypium. — This drug, obtained from the cotton plant, was, I believe, much used by the American slaves to produce abortion. It is supposed to have an action somewhat akin to ergot. I have prescribed it in certain cases of uterine hæmorrhage, thus:

℞	Ext. gossypii radicis corticis (Ind. and Col. adend) .	♏xxx
	Ext. hydrastis liq. . .	♏xv
	Tr. nuc vomic . . .	♏x
	Aqua ad	℥j

As to its results I am not yet in a position to be dogmatic, but it is worth remembering.

Drugs Benefiting Dysmenorrhœa and other Forms of Pelvic pain.

First in this connection one must place the large number of analgesic drugs now at the physician's service. The list has grown enormously since the prototype antipyrin was put on the market a good many years ago. All of them have been used for dysmenorrhœa, but I have had the best results on the whole from phenalgin—an ammonia combination of antipyrin.

Phenalgin is usually prescribed in doses of 5 gr. hourly for four to six consecutive hours. It is specially suitable for those cases of virginal dysmenorrhœa in which the pain is limited to the first few hours or day of the period. Thus:

℞	Phenalgin . . .	gr. v
	Mitte pulves. vi	

One to be taken every hour when the pain comes on.

I often give it with ammonium bromide, thus:

℞	Phenalgin . . .	gr. v
	Ammon. brom. . .	gr. xv

Put up in a cachet, and give one such every hour up to six doses.

In cases where phenalgin does not give relief I try antipyrin, or phenacetin, or some of the other similar drugs in the same manner.

There is one disadvantage attaching to all these analgesics, viz. that after a time their beneficial effects decrease until at last they cease to do any good at all. The reason of this I am ignorant of, but in its event the substitution of another member of the series usually again relieves the pain for a while. Permanent relief of virginal dysmenorrhœa by means of these analgesic drugs never occurs,

dilatation of the cervix by the fœtal head or the mechanical dilator being the surest cure.

The analgesic drugs are of much less service in the acquired forms of dysmenorrhœa, and in chronic pelvic pain not of menstrual origin they are outside the therapeutical picture altogether.

The bromides.—In virginal dysmenorrhœa we have merely pain, and pain for a short period, to treat in most instances. In the acquired or so-called "congestive" dysmenorrhœas, and in the varieties of chronic pelvic pain, this is not so, there being almost invariably some other complaint as well, such as menorrhagia, leucorrhœa, dyspareunia, a general sense of debility, and so on. Thus our prescriptions in such cases usually consist of several drugs administered to these various ends.

First and foremost amongst the therapeutic agents used in these classes of patient are the bromides. And here I would draw your attention to a peculiar therapeutic observation. One of the chief complaints of the women attending a gynæcological clinic is "weakness." If a male patient complained thus we should, in the absence of contra-indicatory physical signs, give him a mixture containing, say, strychnine, dilute acid, and a bitter, and in nine cases out of ten benefit would result.

But I have found that, if you treat a case of gynæcological debility on these lines, the result is invariably disappointing, the patient being either no better or distinctly worse. On the other hand, the administration of potassium bromide is constantly followed by the satisfactory declaration on the part of the patient that "she feels so much stronger." I have therefore quite given up the use of the regular tonics in these cases, and use the bromides instead.

If one may speculate on the reason of this apparent anomaly, I should say that the cause of the "weakness" complained of in the case of a male patient is in most cases primarily physical, with a secondary nervous want of tone, whilst in the case of the woman the sense of ill-being is, in the first instance, due to a hyper-irritability of the nervous system, the steadying of which by the bromides immediately produces a sense of "feeling stronger."

How far this reversed action of strychnine and the bromides is applicable to women suffering from complaints other than those of the genital organs I do not know, but in gynæcological practice I have no doubt of the truth of the observation I have brought to your notice.

Perhaps the most generally useful prescription in the Chelsea Pharmacopœia is the mist. pot. brom. c̄ cinchona.

℞	Pot. bromid. . . .	gr. xx
	Tr. cinchona co. . .	♏xxx
	Aqua chlorof. ad. . .	℥j

It is my first choice in all cases of indefinite pelvic pain uncomplicated by other symptoms, and usually gives more or less satisfaction.

I think the bromides are too often given in insufficient doses. Less than gr. xx is rarely indicated in these patients. I frequently use the sodium or ammonium salt in cases where a general depressant effect is not desirable.

There are two chief combinations with the bromides, viz. ergot and iron, thus:

℞	Ext. ergot liq. . .	♏xxv
	Pot. bromid. . . .	gr. xx
	Aqua chlorof. ad. . .	℥j

and—

	Ferri am. cit. . .	gr. x
	Pot. bromid. . . .	gr. xx
	Aqua chlorof. ad. . .	℥j

The first is useful in the acquired dysmenorrhœas complicated by a degree of menorrhagia; the second I find good in debilitated anæmics complaining of chronic pelvic pain with few or no physical signs.

Guaiacum.—This drug has been warmly recommended by Herman; I gave it a good trial in consequence, but I cannot say I got very good results.

Aletris.—Aletris undoubtedly benefits certain cases of dysmenorrhœa and chronic pelvic pain. I have given it as the well-known "Cordial" with good results, but chiefly in the following combination:

℞	Ext. aletris liq. . .	♏xv
	Tr. bryoniæ . . .	♏x
	Pot. bromid . . .	gr. xx
	Aqua ad	℥j

which has proved very successful. Parke, Davis & Co. also prepare an "elixir" containing it. I commend my prescription to your notice as really useful.

Viburum prunifolium.—Here, again, we have a useful drug. I usually prescribe it in the form of the "Liquor Sedans" (Parke, Davis & Co.), dose

3ss to 3j, but as the liquid extract it may be conjoined in drachm doses with any other of the so-called uterine sedatives.

Salix nigra.—This drug, as the fluid extract in doses of 3ss to 3j, has been recommended in pelvic pain. I have used it, and, I think, occasionally with advantage.

"*Styptol*," "*Stypticine.*"—I have already referred to the pain-quieting effect that these drugs sometimes produce.

Belladonna and Hyoscyamus.—These two drugs are both occasionally useful adjuvants to the other agents used for allaying pelvic pain. Hyoscyamus is the more valuable of the two and is chiefly effective, I have found, in dysmenorrhœa of the spasmodic or intermittent variety. It deserves a trial in such cases.

Drugs useful in Amenorrhœa due to Chlorosis or Genital Insufficiency.

Iron, of course, is the first remedy in these cases. After trying all forms in cases of chlorosis I find the following the most useful, in that, except in cases complicated by very severe gastritis, it can be administered without fear of incommoding the stomach:

℞ Ferri am. cit. . . . gr. x
Liq. strichniæ . . . ♏v
Aqua chlorof. ad. . . . 3j

In many cases it is advisable to spend a week in administering the common white mixture—

℞ Magnes. sulph. . . . 3j
Magnes. carb. . . . gr. x
Aqua menth. pip. ad. . . 3j

three times a day before resorting to it.

Where dyspepsia complicates the case to a marked degree I give, in addition to a strong purge at night, the following:

℞ Bismuth carb. . . . gr. x
Sodii bicarb. . . . gr. xxx
Sp. chloroform . . . ♏xv
Aqua carui ad. . . . 3j

three times a day after meals when the pain begins

For many cases of amenorrhœa, whether due to definite anæmia or some insufficiency of the sexual organs, the old Pil. Aloes c̄ Ferr., three times a day, is difficult to beat.

Apiol, Hellebore, and Savin.—These drugs are supposed to have a specific emmenagogue effect. I have used them all, but chiefly apiol, in the form of the proprietary preparation "Erg-apiol" (Smith), which I think in certain cases is efficient.

Of hellebore and savin (both given as the tinctures in doses of 3ss) my experience is limited to their application to those curious cases of sudden, apparently causeless amenorrhœa in vigorous young women. I cannot say I have had any definite results, but such cases are notoriously hard to treat.

Whilst on this subject I may be perhaps permitted to mention what I consider to be the most generally useful purgative in women's disease; it is:

℞ Ext. cascara sag. . . 3j
Magnes. sulph. . . 3j
Tr. hyoscyamii . . 3ss
Aqua menth. pip. ad . 3j

It is a surprisingly powerful purgative, much more so than one would gather from the ingredients, though individually active and given in full doses.

It can be prescribed in doses varying from a drachm to an ounce, and the patient should be instructed to regulate the amount herself. Its one drawback is that it is rather nasty to the taste.

Drugs Relieving Bladder Irritability.

The subject of the complaints made by women on the score of the vesical function is very complex. Such complaints generally take the form of much pain during or after the act, together with a frequent desire to micturate.

In spite of the formidable list of symptoms vouchsafed by the patient in nine cases out of ten no organic defect can be found, and that this is not due to any gross carelessness on the part of the examiner it may be noted that they disappear as mysteriously as they came on.

I have only time to show you two prescriptions that we find of great use in these cases. They are:

℞ Ammon. benzoate . . gr. xv
Tr. hyoscyamii . . . ♏xxx
Inf. scoparii ad . . . 3j

and—

℞ Pot. citrat. . . . gr. xxx
Pot. bicarb. gr. xv
Tr. hyoscyam. ♏xxx
Inf. buchu ad . . . 3j

Some Topical Applications and Douches.

Finally, I will tell you of certain topical applications and douches that have proved useful in my hands.

In cases of vaginitis a 10 per cent. solution of protargol repeatedly applied through a speculum to the vaginal wall is, I believe, the most efficient means of allaying the inflammation.

Later on in acute cases and at once in chronic cases it is necessary to make direct application to the cervical canal, since this is invariably infected as well, and keeps re-infecting the vagina so long as it continues. This is best done by means of wool soaked in "iodised phenol" (iodine one part, carbolic acid four parts), or pure carbolic acid, and mounted on a Playfair's probe, or, better still, a long and narrow-bladed sinus forceps.

Various medicaments are sometimes applied to the cervix by the vehicle of wool tampons soaked in glycerine. This is a messy way of doing it, and latterly the introduction of soluble vaginal pessaries, such as the "gynecols" of Squire, has improved this form of therapy. They should be introduced overnight and douched out in the morning.

Douches.—For purely antiseptic purposes, in simple cases, boric acid (℥j ad Oj) is probably the best. Where stronger effects are required lysol is very useful (℥ss ad Oj). Mercury solutions, even when dilute, frequently produce irritation after some time, and occasionally symptoms of mercurialism.

If a deodorant is required tr. iodi (℥j ad Oj) is very good, while crude sanitas (℥j ad Oj) is, I think, the best douche for cases presenting much fœtor, as in advanced cancer of the cervix.

For sedative purposes borax (℥j ad Oj) and lead acetate (℥j ad Oj) are excellent.

In the later stages of cervical erosion, with much discharge, and in some forms of chronic vaginitis, more astringent douches are prescribed. Of these I select the following as the most successful: alum (℥j ad Oj) tannic acid (℥j ad Oj) and the Injectio Quercus Co. of the Chelsea Pharmacopœia, which runs thus:

℞ Alum or sulphate of zinc . . .	℥ss
Concentrated solution of oak bark .	℥ss
Aqua ad	Oj

In conclusion let me call your attention to two excellent anti-pruritics. The first is Resinol Ointment, which many of you, no doubt, already know; the other is a fluid known as "Zymocide," made by the Peptenzyme Company. It contains a mixture of many substances, one of the chief being, I think, oil of wintergreen. It should be diluted six times to make a lotion, which, when applied to cases of chronic vulval pruritus, gives results far exceeding anything else I know for this obstinate and distressing condition.

April 19th, 1909.

A CLINICAL LECTURE

ON

THE RESULTS OF NASAL OBSTRUCTION.

Delivered at the London Throat Hospital.

By SOMERVILLE HASTINGS, M.S., F.R.C.S.,
Senior Assistant Surgeon to the Hospital; First Assistant in the Ear and Throat Department at the Middlesex Hospital.

Gentlemen,—This afternoon I want to try and summarise for you the principal results of obstruction to the air-passages in the nose and naso-pharynx.

It is not my intention to make out a list of the causes of this condition, but you will remember adenoids, nasal polypi, hypertrophic rhinitis and deflection of the nasal septum as among the commoner and more important.

Now the trouble in nasal obstruction may come about in two entirely different ways—through mechanical blocking of the air-passages, and by the production of a "septic focus"—and perhaps I had better first of all try and explain what I mean by this last term.

Some diversity of opinion exists as to the function of the adenoid tissue in the pharynx and naso-pharynx. It may of course serve as a sort of natural breeding-ground for the phagocytes that protect us from invading organisms. But it is curious, if this be the case, that its maximum development should coincide with that very period of life in which the liability to infectious diseases is most marked, and that the membrane of diphtheria should be more often found on the tonsils than anywhere else. But whatever may be its original purpose there can be no question that in conditions of hypertrophy and degeneration adenoid tissue has lost the greater part of any antibacterial power it may have previously possessed. It is not improbable also that as the result of the fibrosis following attacks of inflammation—for we have adenoiditis just as we have tonsillitis, though the symptoms are less marked—that the outward passage of phagocytes may be so much obstructed as to be practically abolished. Now the commonest type of adenoid vegetation met with in children is

formed by some three or four vertical bars of soft velvety material with deep clefts between, and if no special mechanism for the destruction of bacteria exists it will easily be seen that the clefts between these bars and the smaller crevices in the bars themselves will form ideal pockets where bacteria of all kinds can live and multiply. We have only to remember how often a foul nasal discharge is the result of adenoids in children to realise that adenoids may be a true "septic focus."

Authorities are by no means unanimous regarding the normal bacterial flora of the nose and naso-pharynx. Some observers have found it sterile in as many as 70 or 80 per cent., but others assert that streptococci and staphylococci are almost constantly present. No doubt the purifying current of air and the action of the cilia of the mucous membrane are important cleansing agents. And when from nasal obstruction this drainage system is interfered with and stagnant pools of discharge are allowed to collect, it will not surprise us to find that organisms increase greatly in numbers, multiply readily and possibly even attain increased virulence.

In one of these ways a centre for the multiplication of bacteria is formed either in the nose or naso-pharynx, and many of the results of nasal obstruction are due rather to this nidus of organisms or "septic focus" than to any mechanical blockage to the air-passages. But although the results of nasal obstruction may be thus produced in two distinct ways it will be more convenient to consider both classes together, taking up the various organs that may be affected *seriatim*.

The facies of nasal obstruction is too well known to require much description. There is no special adenoid face, the type of countenance so common with adenoids being merely the facies of nasal obstruction that has commenced early in life. The vacant expression, open fish-like mouth with drooping lower lip and feeble chin, the snub nose with slit-like vertical anterior nasal orifices and alæ nasi flattened against the septum, and moving hardly at all in respiration, the everted upper lip with naso-labial fold more or less obliterated—all these are characteristic of early nasal obstruction. Now and then a well-marked depression may be seen between the superior and inferior lateral nasal cartilages, and occasionally, more especially if the obstruction is caused by adenoids, enlargement of the posterior cervical glands may be noted, or what may be the result of this—torticollis.

Considerable liability to nasal catarrh and an increased tendency to catch cold results from nasal obstruction. This is doubtless due to the unhealthy condition of the nasal mucous membrane, which makes it more susceptible to microbic infection. Occasionally the discharge is foul and purulent, as in the case of children with adenoids, though it is only right to mention that some such children have no discharge whatever, and their mothers complain that they never require a handkerchief at all. The chronic catarrh, or repeated acute attacks resulting from adenoids, deflected septum or other cause of nasal obstruction gives rise to a hypertrophic condition of the mucous membrane covering the middle and inferior turbinals, which in its turn leads to an increase of the obstruction, or, if the obstruction is anterior, the catarrhal process may spread backwards to the naso-pharynx and give rise to hypertrophy of the lymphoid tissue in this region—in fact, to adenoids. Where the obstruction is extreme or involves mainly the upper regions of the nose, as in the case of polypi, the sense of smell is generally lost, and that of taste becomes impaired also. But it is interesting to note that in anterior obstruction, although very marked, the odour of the food may be carried to the nose by the expiratory current, and flavours may be in this way perceived. Occasionally epistaxis is a prominent symptom. I saw a case of adenoids in an adult a short time since where epistaxis was the only thing complained of.

Deafness is frequently associated with chronic nasal obstruction, especially when this is the result of adenoids, and in deaf-mutism adenoids are present in a large percentage of cases. Chronic progressive deafness with retracted membranes is common in nasal obstruction. The retraction is not, however, the direct result of the negative pressure in the naso-pharynx during inspiration, for it is present during expiration as well. It results from the absorption of the air contained in the middle ear, which is not replaced from the naso-pharynx owing to blockage of the Eustachian tube. The Eustachian obstruction is in turn the result of swelling from catarrh, which catarrh is inflammatory in nature and has spread from some "septic focus." It may be also that imperfect action or weakness of the levator palati and other muscles, which should open the Eustachian tube during deglutition, may

have something to do with it, for the palate is not infrequently imperfectly developed in these cases. Suppurative otitis media, both acute and chronic, is so frequently due to nasal obstruction that it is your first duty to examine for adenoids when a child is brought to you with ear discharge. My own practice is to examine and treat at the same time by the use of a small curette, which removes whatever adenoid tissue may be present, and if none is there gives rise to much less pain than would be caused by an average-sized finger. Mastoid disease may also result from nasal obstruction. I have under my care at the present time a child, æt. 7 months, on whom I operated for a large mastoid abscess with extensive necrosis of bone, the result of a pad of adenoids. It is interesting to note that in this case, as often happens in young children, the middle-ear disease had spread to the mastoid without causing perforation of the membrane, so that no otorrhœa was present.

Very definite changes take place in the architecture of the upper and lower jaws as the result of nasal obstruction in early life. The upper jaw is poorly developed so that the teeth are crowded together, and frequently for want of room the canines are displaced outward. The axis of the teeth is altered, the opposite molars being bent inwards so that the crowns of those on opposite sides of the mouth are nearer together than the roots, while the incisors project forward and protrude between the lips. The shape of the alveolar border is also changed. Instead of being horse-shoe-shaped, as is normal, the arch becomes **V**-shaped and pointed so that the apex of the **V** is formed by the central incisor teeth and the sides run straight back as far as the first molars. The arch of the hard palate is also raised; it is usually Gothic or pointed but sometimes flattened. Less constantly associated with, and probably resulting from, nasal obstruction in early life are a deflection of the nasal septum and a conditon in which the upper and lower incisors cannot be made to come together, called by dentists "open bite." In the lower jaw the changes are similar but less marked. There is the same imperfect development with crowding of the teeth, the **V**-shaped pointed alveolar arch and the change of axis of the teeth, only it is unusual to get the same thrusting forward of the incisors as occurs in the upper jaw.

Now, it is one thing to give a list of the deformities of the jaws the result of nasal obstruction, but quite another matter to explain how these deformities come about. Probably there are several factors to be considered. In the first place, if the nose is not used as an organ of respiration we should expect it to develop imperfectly, and the upper jaw is so closely attached to the nose that we can easily see how a failure in the development of the anterior nares will affect the premaxillary region, and how imperfect development of the antrum will influence the formation of the posterior part of the maxilla. Lateral pressure by the facial muscles has also to be considered. It might at first sight seem a little curious that muscular pressure should exert any appreciable effect on such solid structures as the jaws, but we have to remember that the pressure is continued for a long period. A case described by Dr. Lack, in which a boy suffering from early facial paralysis and adenoids developed deformity of the jaws on one side only, gives what we may call experimental support to this view. Now, if lateral compression be exercised on the alveolar margins one of two things must happen. Either the palate must be pressed up or else the alveolar margins must descend. If the former occurs we are very likely to get some crumpling of the nasal septum and deflected septum may result. If the latter, as the compression is absent anteriorly the condition of "open bite" will probably be produced. The mouth being always open the upper incisor teeth are no longer pressed on by the upper lip, and it is by the lack of this compression, at any rate to some extent, that their undue prominence may be explained. Some consider that deficiency in the normal outward pressure of the tongue and the absence of the mutual compression between the alveolar borders of the upper and lower jaws are also factors in the case.

The mouth being always open the cold, unmoistened air produces a congested irritable condition of the buccal mucous membrane with dryness and furring of the tongue, symptoms usually most complained of after a night's rest. Sometimes the condition spreads to the pharynx and gives rise to recurring attacks of tonsillitis with enlargement of the tonsils, or a dry pharyngitis may be set up, but in other cases the tongue appears to take on the function of the turbinates in warming and

moistening the air and the pharynx remains unaffected. The teeth, particularly the incisors, decay readily. This is partly due to their irregularity allowing particles of food to collect between them, which are with difficulty dislodged, and partly, perhaps, to dryness and exposure of the teeth through the mouth being constantly open. Speech is always affected if the obstruction is at all marked. Usually the absence of nasal resonance gives us toneless, flat, muffled vowel sounds and consonants in which "m," "n," and "ng" are more or less replaced by "b" and "p." Very occasionally, when the obstruction is far forward, the voice has a truly nasal twang. In children the articulation is often imperfect, and stammering and stuttering are not rare. Choking and difficulty in deglutition is common in children also. It is, perhaps, most typically seen in infants with adenoids who are unable to breathe through the nose while feeding, and have constantly to let go the breast to obtain a breath of air. The dyspeptic symptoms so often present must be accounted for by the swallowing of the foul discharge as well as by impairment of general health.

One of the most constant symptoms of nasal obstruction is snoring at night. This is apparently only present when the obstruction is incomplete, so that, as usually happens, even in the most severe cases, some air passes through the nose as well as through the mouth. Then the soft palate vibrating between the two columns of air gives rise to the snoring sound. A harsh, dry, irritable cough, usually worse at night, is very frequently present. It is doubtful how far this is reflex or due to the irritation of the pharyngeal mucous membrane through mouth-breathing. It is also necessary to remember that true laryngitis and bronchitis, acute and chronic, are not infrequently brought about by the inhalation of the unwarmed and unmoistened air. Recurring attacks of bronchitis are frequent in children with adenoids, and may be accompanied by broncho-pneumonia.

Repeated attacks of bronchitis as well as anæmia and impairment of general health cannot but favour the development of consumption in a susceptible subject. It has been pointed out, however, that an impaired percussion note with hollow breathing in the supra-spinous fossæ of young children may be the result of collapse of the lung from obstructed inspiration, and does not necessarily indicate tuberculous disease. Permanent deformity of the chest may result from the same cause. The respiratory obstruction, which is chiefly inspiratory and occurs mainly at night, causes retraction of the lower parts of the chest, and if the ribs are soft a permanent depression in the infra-mammary or xiphisternal regions may result, and give rise to the well-known "pigeon-breast."

As soon as a child with the open mouth of nasal obstruction gets off to sleep the muscles of the base of the tongue, like the musculature generally, begin to relax, and the tongue falls back and obstructs the air-way. Asphyxial symptoms now develop, and the child awakes sufficiently to recover voluntary control of the muscles of the base of the tongue, and the condition is relieved for a time, but recurs again in a few minutes. The result is sweating and cyanosis, restless disturbed sleep, and distressful dreams. The anæmia from imperfect aëration of the blood is often combined with a certain amount of toxæmia from septic absorption, and chronic ill-health and imperfect development in children is bound to follow.

Lastly, we have to consider the mental and reflex effects of chronic nasal obstruction. In this affection difficulty in concentrating the attention and inability to undertake any duty requiring close mental application are constantly complained of. There is often loss of memory and some amount of stupidity. Children are fretful, and soon get tired, and seem to lack sufficient energy for work or play. Adults are irritable and morose, and are unable to transact business in the worst cases. Headache and weakness are often complained of. These symptoms were first definitely associated with nasal obstruction by Guye, of Amsterdam, who attributed them to an obstruction to the lymphatic outflow from the anterior part of the brain the result of circulatory changes in the nasal cavities, and in favour of this view is the fact that they are generally most marked when the obstruction is situated in the ethmoidal region. On the other hand, the existence of lymphatics in the brain is denied altogether by some of the highest anatomical authorities. Of the so-called reflex symptoms, that is, symptoms having a more or less distant connection with nasal obstruction, and, in some cases, relieved by its cure, are nocturnal eneuresis, hay fever and asthma, laryngeal spasm, and neuralgic pain. Some would even add epilepsy and chorea to the above, but there is considerable doubt whether the last two have ever more than an accidental association with the affection.

April 19th, 1909.

AUTO-INOCULATION VERSUS HETERO-INOCULATION* IN THE TREATMENT OF ESTABLISHED INFECTION.†

By DR. E. C. HORT.

(*Continued from page* 16.)

Chart 20 is that of a case of pulmonary tuberculosis with moderate fever, but losing weight and with extending physical signs. *Tubercle bacilli* in the sputum. Until artificial auto-inoculation was begun no improvement took place. At the point marked on the chart a higher rise of temperature was produced by artificial auto-inoculation than had previously been recorded. At intervals further inoculations were given, and steady progress ensued. By the time this chart comes to an end the patient

PULMONARY TUBERCULOSIS.

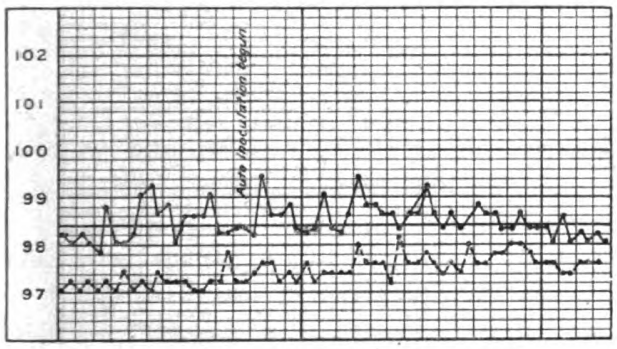

CHART 20.

had lost all cough as well as all physical signs of active disease, and returned home with half a stone to her credit. For the time being the disease is arrested. Auto-inoculations are still being kept up. The absence of the broken curve of declining indices before interference is as marked as its presence afterwards. A continuous morning curve is introduced in this chart, to show the gradual lessening of the excursion between morning and evening temperatures as the patient improved.

Chart 21 is that of a boy with physical signs in both lungs and bacilli in the sputum. In the first month of this chart he had been treated with tuberculin T.R., with apparently nothing but harm. For two months he rapidly lost ground, the disease extending to an alarming extent, especially in the left lung. After the correct dose of auto-inoculation had been arrived at, he received a series of graduated doses through auto-massage of his lungs and rapidly improved, as the chart and present condition of his lung show. He is still under treatment, and though still a source of anxiety, is continuing to do well.

PULMONARY TUBERCULOSIS.

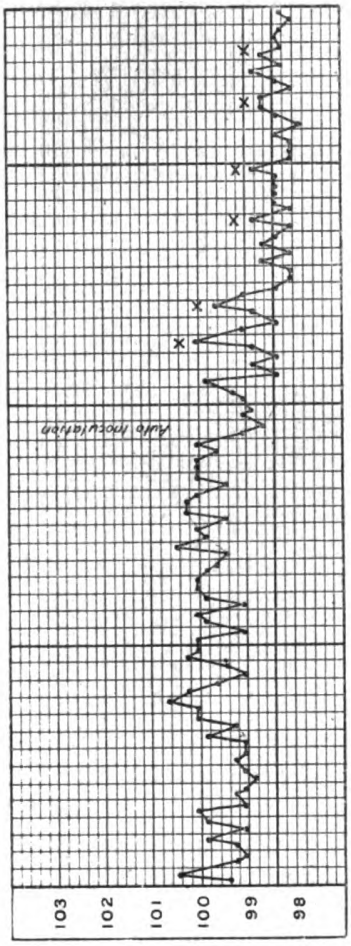

CHART 21.

Chart 22 is that of a severe case of pulmonary tuberculosis. For two months the patient and her temperature chart were carefully watched without any form of specific treatment being given. During these two months she steadily lost ground in spite of absolute rest in bed. At the point marked in the chart auto-inoculation was at last carefully begun. Improvement has been as marked as before it was absent. The patient is still under treatment and there is good hope of eventual arrest. For three weeks after this chart was completed the temperature has improved still further.

* The word "hetero-inoculation" is one that I have coined, from obvious analogies, to denote inoculation of immune serums, and of tuberculin and other vaccines from without.

† Delivered in part before the Royal Society of Medicine.

On two occasions she has in these three weeks been inoculated under the skin with $\frac{1}{500}$ mgr. tuberculin T.R. In both cases the injection has been absolutely ignored so far as clinical manifestations, including temperature, go, as I have frequently observed to happen where the temperature is at or near normal in cases approaching quiescence.

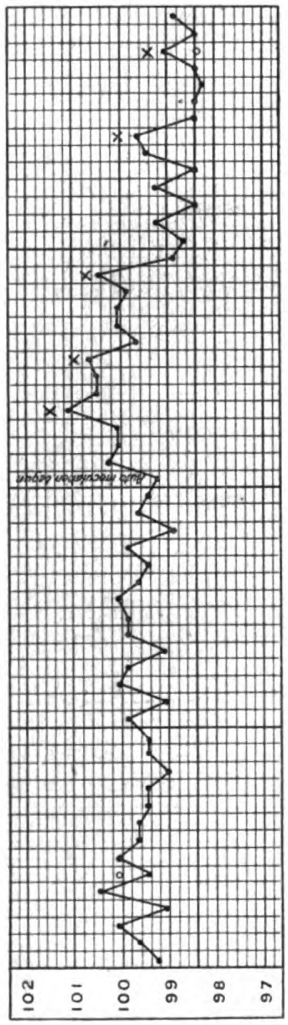

Chart 22.

Chart 23 is worth showing to illustrate the effect of artificial auto-inoculation in a case of influenza complicated by a patch of pneumonia. At the time the artificial auto-inoculations were given the temperature was on each occasion rising. A further rise occurred, apparently as a result of the inoculation, followed in each case by fall. The curve of declining indices after second inoculation is well shown. The physical signs in the lung rapidly cleared, and though convalescence was slow the ultimate result was good.

At this point I wish to summarise the remarks so far made by showing three curves, one of a patient doing well, a second of a patient barely holding his own, and a third of a patient getting progressively worse.

Chart 24 represents a curve moulded from the continuous evening temperature chart of a case of pulmonary tuberculosis that did extremely well without artificial specific aid. In this chart we note that at the point A there has occurred an

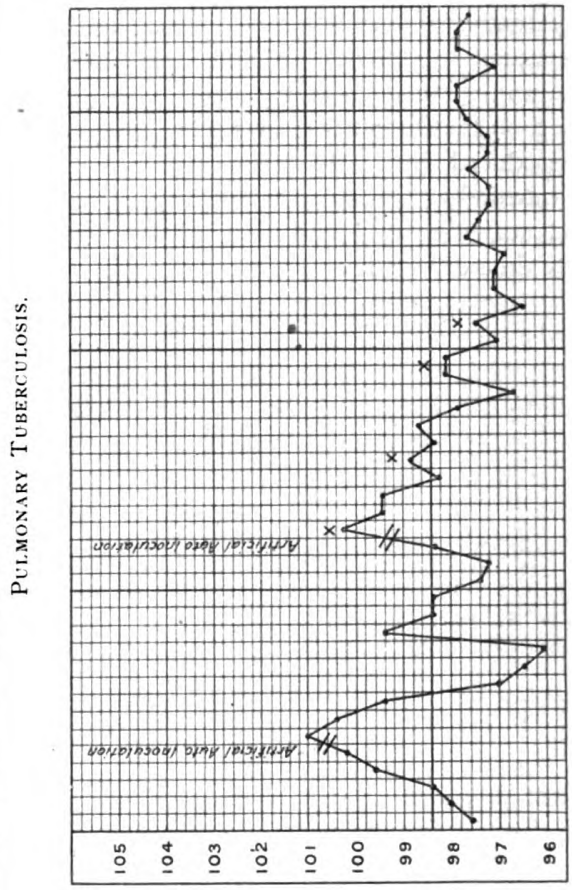

Chart 23.—Three-hourly chart.

intoxication followed by a rise of temperature. The intoxication is followed by an increase of antibody production. This has effectively neutralised the intoxication and a fall of temperature results, as is seen in B C. But the increased protective content called out by the intoxication has done more than merely neutralise it. It has also neutralised or diminished the activity of the area of the focus of disease, which I represent diagrammatically by the large circle A1. When, therefore, the excess production of antibody elicited by the intoxication has worn off the influence of the toxic activity of the infective focus again reasserts itself, but it now proceeds from a smaller and less active focus.

The result, therefore, is that the succeeding intoxication beginning at C produces a less rise of temperature than that beginning at A. The same phenomenon is repeated throughout the curve.

Chart 25 represents a similarly moulded curve

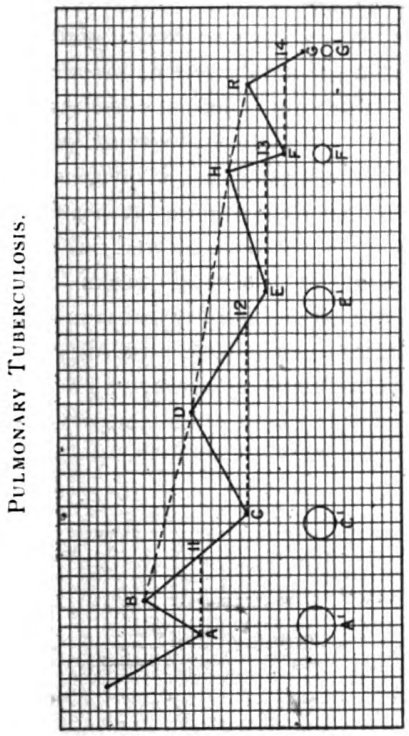

Chart 24.—Intoxication-response curve from continuous evening chart.

from a case of pulmonary tuberculosis in which for many weeks no improvement took place in general conditition or in physical signs. The disease, on the other hand, was not markedly advancing. In this chart we find no increase of antibody production sufficient, as in Chart 24,

Pulmonary Tuberculosis.

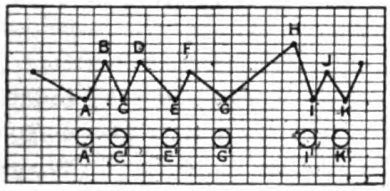

Chart 25.—Intoxication-response curve from continuous evening chart.

sensibly to affect the focus of disease. The only effect of the intoxication is to cause the temperature to rise at A, and when the influence of the antibody production thereby elicited has worn off the temperature returns to its own level. But, as we have seen, there is an insufficient amount of antibody sensibly to reduce the focus of infection. Hence this remains constant, and the temperature again rises to the same height as before. The patient, in fact, is at this stage at a standstill, and unless we can devise some method of eliciting a larger immunity response we cannot look for cure.

Chart 26 represents a curve from a case rapidly going from bad to worse. Here the immunity response has been less than in the two preceding cases; that is, the temperature has not been sensibly reduced in response to the intoxication at A. The focus of disease therefore proceeds to develop unchecked, which is graphically represented in the widening circles drawn. When, therefore, the slight excess of antibody production has worn off, the temperature rises higher than ever from unchecked activity of the disease focus expressed in acuter intoxication.

Pulmonary Tuberculosis.

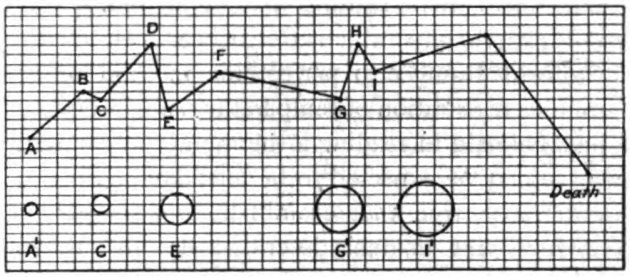

Chart 26.—Intoxication-response curve from continuous evening chart.

The patient died with a pre-mortem fall of temperature, whilst the patient to whom Chart 24 belongs recovered.

In these charts this extension, diminution, or constancy of area of disease is of course purely diagrammatic.

It is not claimed for Charts 24, 25, and 26 that they are anything more than three main types, or that such perfect curves as these will be generally found, if temperature charts are treated in the manner suggested. There are, of course, infinite gradations between the types, and in any one curve there may be from time to time one or more phases of one or other type. I suggest, however, that by careful study of a temperature chart treated in this way, not only in tuberculosis, but also in many other diseases, a predominant tendency to any one type may be of the utmost value in determining both prognosis and treatment.

Charts similar to Charts 1 to 26 may be found in the wards of any hospital, or in the office of any hospital registrar. Perfect examples of the broken curve of declining indices, such as shown, will, of course, only be found as a rule in cases that have been cured, or considerably improved, or at the time of examination are undergoing improvement. The exceptions have already been referred to. Neither, of course, will they be found in cases in which the focus of disease is neither increasing nor proceeding towards arrest, nor in those cases going down hill. Each of these classes have their own peculiar curves. Though the best examples are to be found in chronic tuberculosis, typical charts may often be seen in broncho-pneumonia, measles, smallpox and many other infections. The very prevalence of the types argues strongly in favour of the interpretation suggested. In the acute infections it is necessary to examine three or four hourly charts, or otherwise, in a short infection, the characteristic features may be missed. When the experiments which are being conducted by Professor Gamgee to perfect his method of continuous registration of temperatures are completed, invaluble aid in reading a thermometric immunity curve may be expected to be forthcoming.

If it be true that examination of temperature charts in the manner described can give reliable information as to presence or absence of response to inoculative stimuli it will be clear:

(1) That when taken as a whole the auto-inoculative stimuli, though apparently a succession of isolated inoculations, are in reality potentially continuous. If it were not so the restraining influence of the antibodies, called out by intoxication, would be overcome at some point other than it actually is. In other words, the temperature would at such point rise instead of fall.

(2) That pyrexial cases progressing towards cure afford in many instances an inimitable model for directing our treatment in cases not so progressing.

(3) That cases exhibiting effective response to spontaneous auto-inoculation are not necessarily in need of extraneous specific treatment, whether by tuberculin or by auto-inoculation. Further, that such interference may result in the utmost harm.

(4) That in cases that are obviously going down hill the danger of extraneous artificial treatment is infinitely great, and may only precipitate disaster. In such case if the exhibition of trial doses of tuberculin or of auto-inoculation does not rapidly transform the dangerous type of curve into the type of inclining indices, further specific interference ought to be absolutely prohibited.

(5) That cases doing neither well nor ill are pre-eminently the ones that call for artificial specific aid. In such cases it is a matter of great difficulty to know at what point to insert an inoculative dose. Examination of isolated phases is useless. Even if the results of blood examinations were to be absolutely relied on they can, in pyrexial cases, be of little value in determining at what point to inoculate, unless a curve be plotted out of observations extending over several weeks in such a chronic disease as pulmonary tuberculosis. The possibilities of a thermometric immunity chart may be gauged by the following curve, which is moulded on the temperature chart of a man who had been

PULMONARY TUBERCULOSIS.

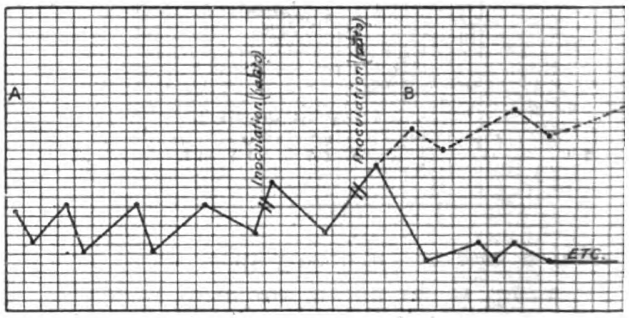

CHART 27.

under observation for many weeks. As Chart 27 shows, he had barely held his own from A to B. Clinically, this was fully borne out in every respect. It was obvious that he could not go on indefinitely in the same way. He was bound to get either better or worse. At the points marked, therefore, I inserted two artificial auto-inoculations by inducing, as in the other cases referred to, artificial hyperæmia of the lungs by making him expire for fifteen minutes through a special form of spirometer adapted for the purpose. The result is admirably reflected in the curve and in the great improvement that ensued. It has since been maintained. The point, however, on which special stress should be laid is this: If the auto-inoculation had not been inserted at the correct phase he might well have been precipitated into the curve represented by the dotted line B-C. The main object of this

chart is, therefore, to show that if the inoculative stimuli shown had not been followed by the curve B–D, to continue with inoculations at any other point than the one selected would have most probably been useless or disastrous. It appears, in fact, if these curves can be taken as a guide, that to insert a stimulus in the response-phase can do no good, though as to this there is not sufficient evidence as yet to make such an assertion definite.

(5) That in a case, as in Chart 24, that exhibits the declining curve of broken indices, and is, therefore, as a result of effective spontaneous auto-inoculation apparently doing well, such terms as "negative" and "positive" phases cannot be applied. The reason for this is that according to such curves each response is an actual positive phase, and each succeeding intoxication a potentially positive phase, as may be seen from its achievement, and therefore only relatively negative.

General Considerations.

What applies in the preceding and following remarks to auto-inoculation applies also *mutatis mutanda* to hetero-inoculation. To get a correct idea of the amount of response called out by any given inoculative measure, examination of isolated phases in a temperature or inoculation chart is of no value. Interpretation of any phase is only possible in the light of many previous and subsequent phases. It is most important that a naturally broken curve of declining indices denoting effective response to spontaneous auto-inoculations should not be mistaken for the results of artificial inoculation. What is often regarded as an instance of correct inoculation is frequently in reality one of hypo-inoculation or no inoculation at all. What is sometimes regarded as an instance of hyper-inoculation may actually be one of correct inoculation. The appearance after inoculation of transient clinical signs, such as headache, malaise, etc., is not necessarily indicative of an excessive dose. When such occur in conjunction with fever, they may be merely the necessary accompaniments of an intoxication essential to effective response. The absence of fever does not argue the inverse. A patient may very well be inoculating himself to good purpose, especially in apyrexial cases, without any change being observable, either clinically or by blood examination. The absence of response as reflected in the blood-stream is said by the opsonists to denote absence of inoculative stimuli. This dictum must be taken with reserve, especially if there is amongst opsonists wide divergence of opinion as to what the opsonic reading of any given serum actually is. In cases of pulmonary tuberculosis doing so well as to justify the view that the focus of disease is relatively quiescent, it can obviously not be possible to exclude the continuance of spontaneous inoculations if improvement in what physical signs remain is observed. In such case, in fact, there must be auto-inoculations going on, in spite of the absence of demonstrable blood change. It is frequently stated that a rise to 99° F. after manual labour or other exercise indicates hyper-auto-inoculation, particularly if the rise be maintained for an hour or more. This statement must be received with caution, as it may mean nothing of the kind. On the contrary, some of the cases of pulmonary tuberculosis which do best are those which for weeks have had high but gradually declining fever as a result of their own auto-inoculations. This point is well shown in Charts 1–5. The benefits of artificial auto-inoculation are, in fact, deliberately confined by some observers to those patients whose temperature is practically normal or even subnormal—in other words, to many of those who are effectively inoculating themselves without artificial specific aid. Many of such cases require no artificial inoculative treatment. The majority of cases of pulmonary tuberculosis without fever do well. There is no difficulty in detecting the minority. Not every rise above 99° F. represents an auto-inoculation. Many intoxications produce a fall in temperature.

It is said that cases of pulmonary tuberculosis in which arrest has occurred are more liable to relapse if they are not then treated with tuberculin than if they are so treated. This may be true, but it is not therefore necessary to submit such cases to treatment with artificial tuberculin. Those whose fortunate experience it has been to watch many patients partially immunise themselves without artificial specific aid, and after return to active life apparently completely immunise themselves against relapse or re-infection by the sole use of their own tuberculin and cell contents, will agree that hetero-inoculation is in such cases an uncalled-for procedure. The argument advanced in favour of the use of artificial tuberculin in such cases is based on a fallacy. The argument is that in a focus

nearly or relatively quiescent auto-inoculations are no longer incitable, and that response must be elicited, therefore, by artificial tuberculin. The fallacy is that, if a lesion be so insulated that auto-inoculation is no longer possible, response to tuberculin administration cannot possibly be conveyed without further procedures, to such lesion. The truth appears to be that until a focus is absolutely insulated, and therefore quiescent, auto-inoculations may still be induced. So long as further progress towards arrest is feasible, as evinced in improvement of physical signs, so long is response not only possible, but probable. There comes a time, of course, in which ordinary auto-inoculations cannot be induced, though unusual effort may incite demonstrable stimulus and response. As Paterson and Turner have well pointed out, the ideal of attainment is the point at which no reasonable labour will provoke inoculation.

ADVANTAGES OF ARTIFICIAL AUTO-INOCULATION.

The merits of artificial auto-inoculation in the treatment of established infection may be thus summarised:

(1) It is based on a natural model of spontaneous auto-inoculation which appears to be responsible for the cure of the vast majority of all cases of infection.

(2) It incites the production of cellulo-tropic bodies, as well as of bacterio-tropic.

(3) It incites the production of antagonising bodies to the toxic products of morbid cell changes.

(4) It incites the production of bodies specific to the particular strain of organism responsible for any given case of infection. For instance, in the case of pulmonary tuberculosis there may be many strains of Koch's bacillus, and therefore a standardised emulsion of new tuberculin or other preparation is not necessarily the correct form to use.

(5) It incites the production of bodies specific to the particular form of cell-enzyme concerned in any given case of infection. Inasmuch as the difficulties of isolation of enzymes and cells for preparation of cellular vaccines are extreme, all such difficulties are obviated by the use of natural vaccines.

(6) If there be a real distinction between bovine and human sources of tuberculosis, the use of artificial auto-inoculation removes both the necessity for establishing the distinction and for meeting the increased difficulties of treatment.

(7) Whenever mixed infections are present it allows for the opportunity of the exhibition of specific antagonising bodies to each and all of the various organisms concerned.

(8) It is free from the danger of adding fresh toxins to those already existing.

(9) It involves no danger of accidental sepsis as with inoculation with artificial vaccines.

(10) It entirely meets the natural and often strong aversion exhibited by the public to artificial inoculative procedures.

(11) It is simple because it obviates the necessity of determining all the organisms concerned in any infection.

It is cheap, because the costly manufacture of often multiple vaccines is avoided.

(12) It co-ordinates all the vast mass of work that has been done in the field of serum and vaccine therapy, and its guiding principle is the same as in methods that have received the sanction of extended trial, though its rationale has not been fully appreciated. Since the practice of hetero-inoculation has become extensive, approved methods of general treatment are in some danger of being deliberately discarded. Auto-inoculation reveals the value of them all, mainly by reason of the attention it calls to the supreme importance of general methods of improving cell-nutrition and cell-restraint.

(13) It renders the difficult problem of dosage incomparably easier than when such agents are laboratory products.

This last statement might be regarded as a paradox, which is, however, more apparent than real. Exponents of the method of inoculation with dead bacilli maintain that by inserting a measured dose of so many million organisms it is possible to get a correct idea of response. Up to a certain point this is no doubt true in infections that are strictly localised and insulated. But whenever artificial vaccines are injected into pyrexial cases, whatever the infection, the case is very different. For in these there is a continuous or intermittent stream of tropins from the infecting bacteria and the cells they have damaged. To add a measured dose of bacteria to an unmeasured dose of bacteria and toxin and an unmeasured dose of cellular toxin, and then expect to get back even a rough response to the whole triad of infection is surely to place expectation high. If, however, it be true, as I submit it may be true, that in pyrexial cases inoculation can be more or less accurately measured by a temperature chart, the measurement of response observed records the sum-total of anti-tropin incited both by damaged cells and their products and by bacteria.

(To be concluded.)

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A LECTURE

ON

DIAGNOSIS AND TREATMENT OF PUS FORMATION IN APPENDICITIS.

Delivered at the Medical Graduates' College and Polyclinic.

By EDRED M. CORNER, M.C., F.R.C.S.,

Surgeon to the Children's Hospital, Great Ormond Street; Surgeon in Charge of Out-patients, St. Thomas's Hospital.

GENTLEMEN,—I selected the subject of appendicitis to discuss with you to-day because it is a very common disease and all see it. Further than that, I see a large number of these cases, and this part of the subject of appendicitis is one which to me has always been one of great interest. It is to put my contention before you and show you that it has important clinical bearings and a valuable treatment, that I selected the subject. In the short time at our disposal I cannot go fully into the details. The elementary details are in the lectures which I gave at the Royal College of Surgeons in 1904,* and which with your permission I will assume, and speak to you about the general points.

The first point which I wish to impress upon you is that the ileo-cæcal region, the neighbourhood of the appendix, is the region in the whole of the alimentary canal which is absolutely packed with organisms. Our ileo-cæcal region has more micro-organisms by hundreds and thousands than any other part of the alimentary tract. Where organisms collect you must expect inflammation to occur; and, as a corollary, where organisms collect there will you find that Nature has disposed the resisting agencies of the body. For instance, our ileo-cæcal region is endowed very largely with lymphoid

* 'Clinical and Pathological Observations in Acute Abdominal Disease,' Constable & Co.

tissue, the object of which being the formation of leucocytes to contend with those micro-organisms. It is in that sense, namely, that it has acquired a large quantity of lymphoid tissue, that our atrophying appendix has acquired a new function. For practical purposes the sole value of retaining the appendix, as has been recently urged, is in the lymphoid tissue, and in nothing else. A little has been said about the secretion from the glands of the appendix; but that can be nothing compared with the millions of similar glands which we have in our intestines; so that the secretion from the appendix can be of little value; but the lymphoid tissue may be of the greatest value.

If the meconium in the intestines of the newly-born baby is examined bacteriologically, we find that it is sterile. So that we may say that not only have we an education for our minds and an education for our bodies, but we also have an education for our intestinal tract, which is largely bacteriological, attaining its maximum in the intestines of gourmets, who can take all kinds of decaying substances without harm. But if you fed a baby with, say, extract of high stilton cheese, it would probably kill that baby, for the reason that the baby has not become immune through its intestinal education. All this is merely a preliminary. I want you to understand that micro-organisms congregate in our ileo-cæcal region in numbers far beyond what they are in any other part of the alimentary tract. In connection with that the lymphoid tissue is also congregated in the ileo-cæcal region, the result of this conjunction being that we have attacks of inflammation in the ileo-cæcal region, which show themselves as appendicitis. Whenever acute inflammation is conjoined with the presence of myriads of active organisms, you may be absolutely certain to get suppuration. It has been laid down by a great authority that if acute inflammation, apart from the presence of micro-organisms, lasts for four or five days you are sure to have pus formation. If you get that acute inflammation conjoined with the presence of myriads of micro-organisms you are absolutely certain to have the formation of pus, suppuration, so that I would strongly emphasise the point that in appendicitis pus formation is almost universal. As the infection occurs from within the appendix, it is quite obvious that the suppuration will also occur inside the appendix, through which pus will be discharged into the cæcum. But I should press the point that pus formation in appendicitis, often discharging into the bowel, is practically universal. It is to that that appendicitis owes its very great danger to life. Unless this is accepted one is apt to under-estimate the danger. With regard to the pathology of appendicitis the formation of pus is almost universal. In those cases, which have been called "medical appendicitis," where the disease is treated successfully by physicians and after a few days of fever the temperature goes down, I contend that there is pus and that it is discharged internally, probably through the lumen of the appendix.

With regard to the clinical features which will assist in giving a prognosis in diagnosing or in treating a case, I would assert that the most important point is the *duration of the fever*. We will return to the definition which was given, namely, that in cases where there was acute inflammation, even without the presence of micro-organisms for four to five days, there would be pus formation. If the temperature in appendicitis is up for as long as four days you can be absolutely certain that there is pus formation. So that as the point of most importance I would put the duration of the fever. There is a further point about the fever. I was very interested in a case, which will be mentioned later if there is time, in which the *character of the fever* helped in the diagnosis. But to return to the clinical features which are of assistance in understanding and treating a case of appendicitis, I will come to the second point. The first one was the fever. The second is the appearance of the *mass in the abdomen*. You have felt many of these cases and know that the lump consists of inflamed cæcum, coils of bowel, and omentum stuck together by lymph. Although you may have felt a large number of these masses in the abdomen in appendicitis, although you know of what it consists, yet I doubt very much whether it has ever been pointed out to you what is the significance of that lump. It is all very well telling us to feel the lump and what it consists of, but it is much more important for us to know what it means. Why is it that these viscera have got stuck together? and why is it that the omentum has closed around so as to form a mass? My contention is that whenever you feel a lump in the abdomen you can be absolutely certain of pus formation. But we can learn more from that lump.

For instance, we will suppose first of all that the pus in that lump is pent up and cannot escape. Then you will find that the lump is an indefinite thing. It is indefinite because the abdominal wall over it is kept in a condition of rigidity, and on account of that rigidity you cannot feel very distinctly the mass underneath. You feel a great resistance, a mass with indistinct outlines, and dulness on percussion. If you find such a mass in the abdomen with such characteristics associated with a rising temperature, a rising pulse, or a high or increasing leucocytosis, then you will know that there is pus pent up inside that mass.

There is another set of characteristics which this mass in the abdomen has. Say, for instance, that the pus in this mass is discharging adequately—and it does not matter how it discharges adequately, either through the appendix or otherwise, so long as it discharges quite freely, then you find quite a different mass. You find that the abdominal wall over the mass is more or less soft, the mass is not tender, and instead of being able to feel it indistinctly it has definite margins, and you can dip your fingers in and define the edges. So that the character of that mass in the abdomen is quite different to when the pus is pent up. Therefore I would strongly urge in cases of appendicitis that if a mass in the abdomen be present, attention should be given to the varying characters of that mass because it will tell you what is happening underneath. If the pus is discharging adequately you leave the case alone. If, on the other hand, the pus is discharging inadequately then you find the indistinct tender mass in the abdomen, associated with fever, a rapid pulse and so forth. If the pus is pent up you have to operate and make an incision, but so long as the mass in the abdomen has the character such as when the pus is discharging adequately then there is no need for any surgical treatment at all.

What I have told you is all very well, but in practice it has one little difficulty. If you watch a mass in the abdomen in a case of appendicitis from day to day, or night and morning, instead of having the characters associated with pent-up pus or the characters associated with an adequate discharge of pus you will find that this mass frequently has a bit of both, leaving one in doubt as to whether the appendicitis will subside by medical means or whether it will require surgical intervention. In such cases I would recommend that you continue to watch this mass and the symptoms associated with it carefully, and if you find symptoms of pain or pus persisting it is a case for surgical interference. If, on the other hand, you find the mass assuming the characters of adequately discharging pus with general improvement, then continue with medical treatment. The long persistence of a mass in the abdomen is really rather a serious thing because it means a lot of adhesions formed there, and if the patient gets over the appendicitis these adhesions may give rise to pain and perhaps to intestinal obstruction.

I scarcely think that it is needful here in the short time at our disposal to discuss the means by which it has been found that pus escapes in appendicitis. It must suffice to say that far and away the most common channel by which the pus in appendicitis makes its escape is *via* the appendix. The pus will find its way *via* the appendix so long as the suppuration is inside the appendix. But if the suppuration, which starts inside, comes outside the appendix then the most common place for the abscess to discharge is through the small bowel. I took the opportunity of carefully examining the walls of some twenty odd appendix abscesses, and was able to demonstrate by means of a probe the perforations in the bowel wall which connected the interior of the bowel with the abscess cavity. After the small bowel, the cæcum is the next most common place for the discharge of an abscess. Beyond that we get rarities, such as discharge into the bladder, into the vagina, and so forth.

In connection with this, and to show you that what I have been telling you is not mere theory composed in the armchair, but really practical, I thought it was better to avoid details and be able to talk over with you some illustrative cases.

The first which I should like to mention to you is one that I saw only this afternoon—in fact I came straight from the Children's Hospital, Great Ormond Street, to here. Earlier in the afternoon a little girl, æt. 9 years, had been admitted into my ward. She had been ill three and a half days. There had been sickness, but that had passed off. But the thing that struck one's attention most forcibly was the child's temperature; it was 101·8° F. and it had been lower the day before. So that the first point that struck one was not only a high temperature, but a rising temperature occur-

ring after an illness of about three and a half days. The next thing one noticed was that the child had a rapid pulse; the pulse was about 110. But although she had this temperature and rapid pulse she seemed perfectly well and talked quite brightly and nicely. When one examined her abdomen one could feel practically nothing but a tense abdominal wall in the region of the right iliac fossa. It was too tender to feel anything underneath, and one could ascertain nothing further than some dulness on percussion in the same region. It was on what I have told you of the characters of appendicitis that the diagnosis was made that pent-up pus was present. Then one took the girl to the operating theatre, and what is really quite a by-the-way item, spinal anæsthesia was used and the operation done. As soon as the spinal anæsthesia acted her abdominal walls were relaxed and she lost sensation; I could feel that there was quite a big lump in her abdomen. But before the anæsthetic acted nothing could be made out except a rigid abdominal wall. At the operation a lot of pus was found. Her case shows that the principles which I have put before you have value in practice.

Another case was one that I had last summer. It was a woman, æt. 39 years, and this was her first attack of appendicitis. The attack began with pain in the right iliac fossa and sickness, subsiding under the care of a physician. It was from the physician's care that the case was transferred to have the appendix removed in what was called a quiet interval. But when one came to examine the clinical features there was no doubt that it was not a quiet interval. The main point which one had for concluding that the operation on this woman would not be an operation in a quiet interval was the character of the temperature. When she first came under my care the acute attack of appendicitis was supposed to have passed off for fourteen days. Yet when I saw her her temperature had not normal characters. A normal temperature should vary about half a degree day and night, but in her case it varied from 97·5° F. to 99·5° F. I have always had a great admiration for our professional forefathers, because they had not the means of modern surgery at their disposal to ascertain what was happening in a particular case. In consequence they gave great attention to clinical detail. The character of the temperature chart is purely and absolutely an instance of clinical detail. I told you that this woman was transferred to my care after her attack of appendicitis had been supposed to be over for a fortnight. I saw this temperature and kept her waiting another week—there was no urgency about the case in any way at all, and one was not endangering her in any way by doing so. All the week that I watched her the temperature kept the same character, varying from between the limits of 97·5° F. and 99·6° F., and it showed no tendency to settle. On examination there was deep tenderness but no mass in the abdomen. Yet from the character and duration of the temperature one felt that there was pus pent up. The question was, where? The temperature showed no sign of declining, so operation was undertaken. As the appendix was being removed the cause was found. Her appendix was full of pus. The appendix had no stricture, so that the pus was discharging from time to time into the cæcum. But the suppurative process which had given rise to the appendicitis was still active. Her medical attendant had thought that the attack of appendicitis had ceased, but really it had not ceased, the suppuration, which I contend is almost universal in appendicitis, continuing, and the pus discharging into the cæcum, so that the woman's temperature went up as high as 99·5° F. at night. At the operation, then, one was able to ascertain what was the true explanation of the clinical features.

Another case—I think it was last summer—was that of a woman, æt. 20 years. She had her first attack. She had been in bed a fortnight and had had pain, but no sickness. Since that attack, which was "nine months ago," she had had repeated attacks, the duration of these attacks varying to three days and never beyond that. It is noteworthy that the attacks were always a great deal worse at her periods. There was no sickness in any attack and she suffered from constipation. This had been going on for nine months. When operated on a thickened appendix was found; there were some adhesions, there was no stricture and no concretion. That being so, what was the cause of her symptoms? The first attack kept her in bed fourteen days, of which she had temperature for about eight or nine days. On my interpretation, she had a formation of pus in that first attack. What, then, is the explanation of those

frequently repeated little attacks lasting three days? I would suggest that during the whole course of her illness there was a certain amount of suppuration going on inside the appendix, and that the subsequent attacks marked the times when the pus did not discharge freely through the appendix into the cæcum. If there was a temporary block, such as with the increased pelvic vascularity of the periods, the pus might not escape freely from the appendix into the cæcum. That is the explanation of those frequently repeated attacks. The appendicitic suppuration was going on the whole time, and the exacerbations were due to the pus not having a free escape. It is consonant that we find the appendix with no concretion, with no stricture, and only thickened and with only a few adhesions. As soon as that was removed this woman never had any more attacks. That is the third case in which you will see the practical bearing of my suggestion.

I have cards of two more cases which I will mention very quickly. One is a man, æt. 29 years, who was a relieving officer. He had two attacks of appendicitis without sickness. After the first attack he was in bed seven days, and after the next he was in bed fourteen days. The man said that on each occasion he had a lump in his right iliac fossa. That lump the man did not feel in the acute stage, but only during convalescence. That is the mass which remained from inadequately discharging pus. In his case, although he had had those two attacks of appendicitis and both had subsided under medical treatment, one was able to prove that he had had an appendix abscess, because at the operation a perforation was formed into the cæcum, which was sewn up, definitely proving that the abscess had discharged into the cæcum, and bearing out my contention that there is pus formation in cases of appendicitis which subside under medical treatment.

The last case is that of a girl, æt. 15 years. She had three attacks. The first was slight and the second was very severe; apparently she was in bed for nine weeks. In that case we know for certain that there was an abscess, because it discharged into the bowel. What her case teaches is this: that there is a case of appendicitis in which we know there has been an abscess, because that abscess has discharged *per rectum* and we have seen the pus. I operated on that girl some little time afterwards—I cannot say at present how long. You would expect, as we know for a certainty that the abscess discharged through the bowel, that we should find a perforation through which that pus had discharged. But nothing of the sort. The appendix, which is described as five inches long, was removed. It was bound down with the adhesion to the pelvic viscera; there was a concretion present and two strictures, but there was no perforation into the bowel of any kind whatsoever. So that this case definitely proves to you that the pus that forms in cases of appendicitis, which subsides under medical treatment, may discharge into the bowel, and if you only allow sufficient time to elapse between the attack and your operation the hole in the bowel through which the pus discharges will become closed.

These are the practical lessons which one has chosen to bring before you. One could bring a number of others. Almost every case of appendicitis that one has to do with teaches some lesson. I can tell you that, since I have adopted these ideas of pus formation in appendicitis, I have learnt infinitely more about the disease and its treatment than I had by the ordinary teaching, in which nothing very definite was said about the character of the attack, and practically no explanation of the clinical features of the cases was offered, such as—why the temperature kept up so long, why in some cases we get a lump in the abdomen, why we get adhesions, or why it is that some people with an attack of appendicitis have continuous pain and discomfort, and why some have recurrent attacks. We found that the earlier teaching about appendicitis offered no explanation of those conditions. It was when the idea was adopted that appendicitis was definitely a septic disease caused by micro-organisms, and that suppuration was almost universal in it—it was then that one began to learn.

In closing I will just read you a few lines giving the conclusions which one has formulated on another occasion.* (1) Suppuration is almost universal in appendicitis; (2) in cases recovering without the need of operation the pus is discharging almost always by the appendix; (3) if the temperature is raised for as long as four days, pus is present; if there is a mass in the abdomen, pus is present. When pus is present it often discharges satisfactorily internally, about three times as often into the small as into the large bowel; (4) temporary fæcal fistulæ are common after opening appendix abscesses; of that I have not time to put forward any illustrations, but may refer to a former lecture†; (5) "if such fistulæ communicate with a hollow viscus and persist, there is great danger in the operation of appendicectomy done

* Before the Harveian Society, 1908; 'Medical Press and Circular,' December 9th, 1908.

† Clinical Journal, August 24th, 1904.

in a quiet interval." This is really a very important point, in which connection I should like to have told you of some cases. Suppose a man has had a severe attack of appendicitis and been in bed a fortnight or three weeks. If one operates on that case in a so-called quiet interval, going fairly at it, if all goes well you are apt to think youself a fine fellow, for it is unusual for such cases to do anything but go right. It is really when you get cases that do not go right that you begin to learn. I remember operating on a man who had been laid up on and off for four months with appendicitis. One operated on him and removed the appendix with ease. The man went on all right for about thirty-six hours and then he began to get uncomfortable; it was not very definite. Then he got still more uncomfortable, and to cut a long story short he died of general peritonitis. I was so impressed with the apparent ease of the operation and the disastrous result that I examined the abdomen after death to find out what really had happened. Then the truth was discovered: there was a hole in his cæcum. Not a hole in his cæcum where I had removed the appendix—that was all right; but above that and on the outer side there was a perforation in the cæcum. I thought, Had I torn that? But when one came to look at it one found that this hole in the cæcum had smooth round edges such as are associated with an old chronic perforation. Then I looked at the appendix which I had removed, and there one found a similar round old hole which had never been noticed. That was the first case which thrust it on me that the pus formation in cases of appendicitis, which subsides under medical treatment, may leave behind it fistulæ—that is, communications with a hollow viscus. If you remove the appendix without due care, you may leave the hole in the bowel open with the result that the patient gets general peritonitis. Since that date I have seen several such cases, but I have lost only one; it was a case of the late Dr. Cullingworth's, in which, again, post mortem there was found a perforation of the cæcum.

The final contention which one would urge is: that appendicitis owes its danger to life to its septic character; that the presence of pus is not necessarily an indication for operation; and that its presence is almost universal in the disease. I recognise that these pus formations in appendicitis may discharge internally perfectly satisfactorily, and if they do so it is better that they should do so. Recognising that, I do not urge that surgical intervention is necessary in every case of appendicitis. But I do assert that surgical intervention is necessary where there are symptoms of pent-up pus, or an inadequately discharging pus formation, in the appendix. If the discharge is adequate then surgical intervention is unnecessary.

April 26th, 1909.

RED DEGENERATION OF UTERINE FIBRO-MYOMATA.

By FRANK E. TAYLOR, M.A., M.D., F.R.C.S., M.R.C.P., D.P.H.,

Gynæcologist to the Hampstead General and North-West London Hospitals; Obstetric Registrar and Tutor to the Middlesex Hospital; Late Pathologist to the Chelsea Hospital for Women.

UTERINE fibro-myomata are subject to many forms of degeneration—malignant, infective, œdematous, myxomatous, calcareous, necrotic, necrobiotic, fatty and amyloid. Of all these degenerative changes none gives rise to appearances so striking and characteristic as those produced by that variety of necrosis known as aseptic necrobiosis or red degeneration.

As a result of this process, a hard, pearly white, whorled, odourless fibro-myoma becomes transformed into a soft, fleshy mass, deep, reddish-brown or mahogany-red in colour, and of a stale fish-like odour reminiscent of the amines. In a well-marked example the cut surface of the tumour presents a homogeneous deep red colour, having quite lost its characteristic whorling. This appearance has suggested to the minds of various observers a resemblance to liver or to raw beef steak, and this latter resemblance is still further enhanced by the fact that the freshly cut surface tends to become darker on exposure, whilst the original colour retained by the deeper parts is readily restored to those parts when a fresh section is made. In less marked cases the periphery of the tumour may have escaped the degenerative process; it will then retain its original white whorled appearance, and the central portion only will show this red degeneration, whilst in still slighter cases only a red or pink staining of the tissues of the fibro-myoma is observable.

In the most advanced cases, on the other hand, the central parts of the tumour may soften and break down into a brownish-red mucoid fluid, or a red pulp. It may readily be conceived that this pulpy fluid may become absorbed, and the peripheral portions of the tumour may then undergo similar softening and absorption, leading to the ultimate absorption and complete disappearance of the whole fibro-myomatous tissue.

The necrobiotic change is thus seen to commence in the central portions of the tumour, where

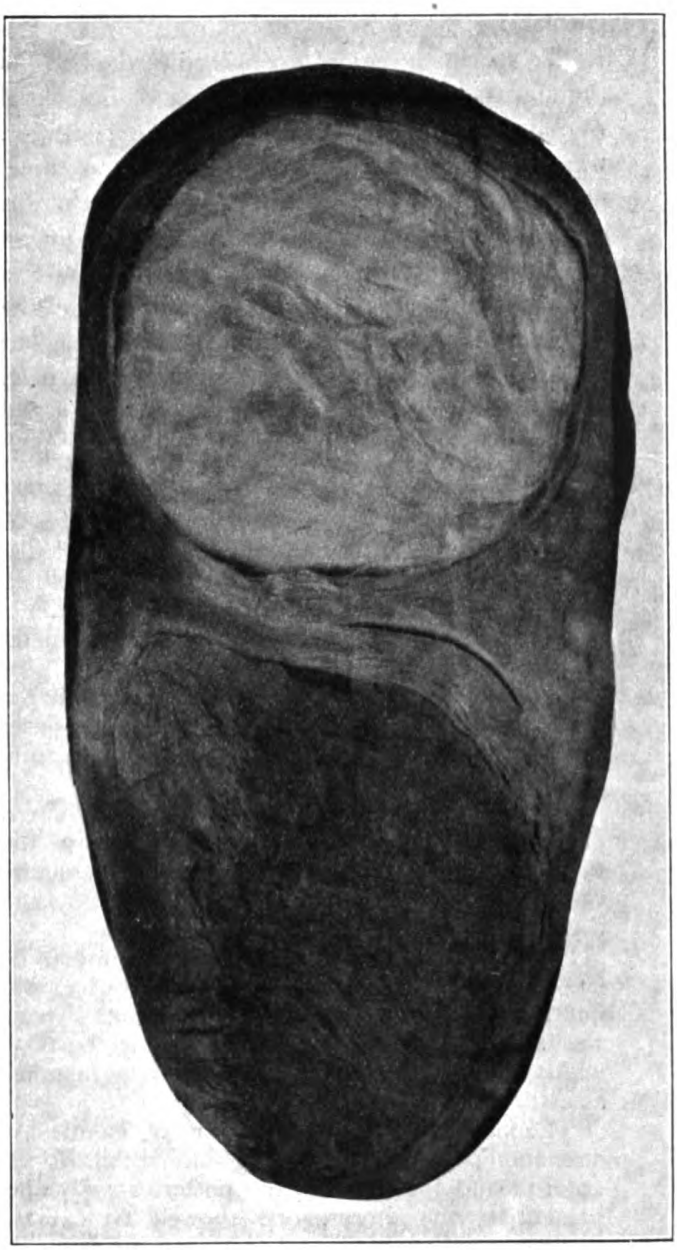
it is usually most marked, although the whole tumour may present a uniformly red colour. It may commence either as irregular streaks, as scattered, isolated, rounded foci, or as a uniform pinkish staining of the tissues of the fibro-myoma.

The histological appearances are thus described by Fairbairn: There is a marked deficiency in the nuclear staining of the tissue cells, and in the more advanced cases this results in an almost entire absence of nuclei in the section, leaving only wavy bundles of fibres which take up the ground stain. In places where the nuclei have taken up the stain they appear much more faint than usual, and fully merit the title of "nuclear ghosts." In some cases the muscle bundles show signs of granular or hyaline changes.

Of late much attention has been bestowed upon the degenerative changes to which fibro-myomata are liable, and red degeneration is one of the commoner forms, for, as I have recently shown,* it occurs in about 6 per cent. of all uterine fibro-myomata submitted to operation.

In the following case the uterus contained two large interstitial fibro-myomata in the anterior and posterior wall respectively, one of which showed the characteristic mahogany colour of red degeneration, whilst the other showed the white pearly colour of undegenerated fibro-myoma. The presence of both in one uterus afforded a striking contrast.

The history of the case runs thus: H. B—, æt. 45 years, was admitted into Chelsea Hospital for Women under the care of Dr. A. E. Giles on January 8th, 1909, complaining of abdominal pain and swelling. Married twenty-one years she has had three children, the last seventeen years ago. The patient had been ailing since November, 1906, when she had a severe attack of pain in the lower abdomen which confined her to bed for three weeks. Since then there has been a gradual and progressive enlargement of the abdomen. Menstruation has been very irregular and scanty for the last two years, there being amenorrhœa for six months, which was terminated three weeks ago by the appearance of a scanty pink flow lasting two days. Notwithstanding the presence of abdominal pain the patient was able to keep about until quite recently, when she was again confined to bed for two weeks on account of an attack of severe abdominal pain. She has also had much bearing-down pain. In December last there was retention of urine, on one occasion necessitating the passage of a catheter. The bowels were relaxed. During her present illness the patient has suffered from dyspepsia and has lost flesh.



On examination a rounded, firm mass was felt rising from the pelvis into the right iliac region and extending upwards to within one and a half inches of the umbilicus, and a second swelling was felt on the left side lower down and of less firm consistence. The cervix was drawn high up in the

* Taylor, Frank E., 'The Lancet,' 1904, vol. ii, p. 83.

pelvis and was small, and the connection of the tumours with the uterus was somewhat obscure.

On January 11th cœliotomy was performed, the uterus and fibroids being removed by supra-vaginal hysterectomy, the left uterine appendages being also removed. During convalescence symptoms of intestinal obstruction developed, but were overcome by the administration of purgative enemata.

The specimen removed consisted of the body of the uterus enlarged by the presence of interstitial fibroids, together with the left uterine appendages, which were normal. It weighed four and three-quarter pounds. In the posterior wall of the uterus was a globular fibro-myoma measuring four inches in diameter, encapsuled, softish, and of a uniform mahogany red colour. In the anterior wall of the uterus was also a globular fibro-myoma of four inches diameter, hard, white, whorled, and free from any sign of degeneration. The uterine cavity was not encroached upon by either tumour, and the endometrium was not thickened.

Histologically the red fibro-myoma showed loss of the outlines of the muscle-fibres, with feeble diffuse staining, with nuclear "ghosts" and disappearance of the nuclei, and the white fibro-myoma was composed of normal fibro-muscular tissue.

The association of pregnancy with red degeneration has been dwelt upon by several observers.* In this case the last pregnancy had occurred seventeen years previously, and fifteen years before the onset of symptoms, being too remote to have any significance.

The symptoms usually present in cases of red degeneration are pain and tenderness in the tumours together with a raised temperature and cachexia from absorption of toxic products from the degenerated tissue.

Pain, as detailed above, was the most marked feature of this case; tenderness, however, was not elicited by palpation of the tumour. Pyrexia was absent during the patient's stay in hospital, whilst loss of flesh during the illness may be taken as evidence of cachexia.

The fact that of two fibro-myomata, identical in size and position (one being interstitial in the anterior and the other in the posterior wall) were present in one uterus, one showed typical red degeneration while the other was normal, could only be accounted for on the assumption that some local nutritional disturbance in the degenerated tumour was responsible for this condition.

Lorrain Smith and Fletcher Shaw, from a study of four specimens, have ascribed red degeneration of uterine fibro-myomata to thrombosis of the vessels of the tumour. This I believe only occurs in the great minority of cases, for it was present in only a few of the thirty specimens of red degeneration I have examined, in one or two cases being also accompanied by extravasation of the red blood-corpuscles amongst the tissues of the tumour. In the majority of the specimens neither thrombosis nor hæmorrhagic extravasation could be observed.

Further, the suggestion that some infective micro-organism is the cause of this form of degeneration is negatived by the fact that repeated inoculations of culture media have invariably remained sterile.

I have also endeavoured to ascertain the nature of the colouring matter present by expressing the tissue pieces in a muscle press, and, after suitable dilution, examining spectroscopically the fluid so obtained. The two-banded spectrum of oxy-hæmoglobin is seen under these conditions, and it is replaced by the one-banded spectrum of reduced hæmoglobin on the addition of such reducing agents as Stokes' fluid or ammonium sulphide.

It may therefore be concluded that red degeneration of uterine fibro-myomata is an aseptic necrobiosis of the tumour cells associated with a diffuse staining of the tissues with hæmoglobin, due to some local disturbance of nutrition in which pregnancy often, but by no means invariably, plays a part.

April 26th, 1909.

* See Taylor, Frank E., 'The Practitioner,' June, 1906.

AUTO-INOCULATION VERSUS HETERO-INOCULATION.* IN THE TREATMENT OF ESTABLISHED INFECTION.†

By Dr. E. C. HORT.

(*Concluded from page* 32.)

Autolysis, Autolytic Toxæmia, anti-Autolytic Defence; the Anti-tryptic Index.

For a complete survey of work already done on such subjects reference must be made to publications by Opie, Cathcart, Wiener, Müller, Koltschmann, von Dungern, Levene, Wells, Stookey, Hill, Schryver, and many others. Here only the most salient points can be touched on with the object of showing the nature of autolysis and of anti-autolytic

* The word "hetero-inoculation" is one that I have coined, from obvious analogies, to denote inoculation of immune serums, and of tuberculin and other vaccines from without.

† Delivered in part before the Royal Society of Medicine.

defence. A study of these will incidentally throw light on their relation to the protective measures employed by the economy to antagonise other forms of cell aberration.

(1) *Autolysis.*—All the known work on autolysis is based on observations made in 1871, when Hoppe-Seyler indicated the resemblance that we now know to exist between the action of the digestive ferments and non-putrefactive solution of dead tissue *in vivo*.

In 1890 Salkowsky (5) showed that this liquefaction was due to the digestive action of intra-cellular enzymes with by-production of leucine and tyrosine. In 1900 Jacoby (6) gave the name of autolysis to the process of self-digestion by intra-cellular enzymes noticed by Salkowsky. As is well known, this observer's fundamental experiment was to pound a specimen of liver and to add toluol or some similar antiseptic. In twenty days digestive changes were demonstrated, the control of course being heated to destroy its enzymes. The rate and extent of autolysis were then determined by estimating the nitrogen content of the coagulable and the non-coagulable residue. Autolysis seems in general to be effected by the combined action of lytic enzymes liberated from the tissues themselves and of hetero-autolytic enzymes liberated from other cells, particularly leucocytes. Since 1900 a host of observers have shown that there is no body cell or tissue which cannot digest itself under appropriate conditions, either *in vitro* or *in vivo*. The rate and extent of autolysis varies in different tissues. Liver-cells autolyse apparently quicker than any other, while vascular endothelium is the slowest. The intra-cellular enzymes responsible for autolysis are endowed with the power of lysis not only of proteins but also of glycogen, lecithin, fats, sugar, etc. The autolytic enzymes of each kind of cell appear to be more or less specific, with the exception of enzymes from leucocytes, which seem, as is generally recognised, to be capable of almost universal proteolysis. For a time autolytic enzymes were supposed to have only lytic functions. Soon, however, it became clear that it was not possible to exclude the probability of their having synthetic properties as well as lytic, and so they were called proteases, lipases, etc.

(2) *Toxicity of enzymes.*—In 1890 Hildebrandt (7) published his observations on the toxicity of certain secreted enzymes, such as pepsin, diastase, rennin, etc., when injected into animals. In the following year it was shown by Achalme that the toxic effects produced were not due to bacterial infection; for by injecting only enzymes that had been sterilised (*sic*) by filtration through porcelain, he obtained the same symptoms of toxæmia.

In connection with the discovery of the toxic effects of enzymes there are many striking points of resemblance between non-bacterial enzymes and toxins. Enzymes are not destroyed by low temperatures, not even by liquid air, nor are toxins. Both are most active between 35° C. and 45° C. There is a further apparent similarity in their behaviour in that they may both be accused of possessing a haptophore group and a toxophore, the former combining before the latter can become active. Again, immunity to their action may be produced by receptors capable of combining their haptophore groups, thus giving rise to anti-ferments. Horschan claims that he has produced an anti-rennin, also a fermentoid. On the other hand enzymes are more heat-labile than bacterial toxins, and do not produce their effect according to the law of definite proportion. Both are very difficult to isolate in anything approaching a pure condition; neither will stand boiling, both resist dry heat of over 100° C., and both on standing lose something of their toxicity.

(3) *Specific anti-enzymes.*—The basis of all subsequent work on anti-enzyme production is, of course, Calmette's and Sir T. Fraser's well-known work in 1893 and 1894, when they first immunised animals against the salivary enzymes of poisonous snakes. Shortly after this it was shown by Hildebrandt (30) that animals could be immunised against emulsin, and that their serum when so treated restrained the action of diastase. It is of interest to note that it was Hildebrandt who first succeeded in producing immunity by the method of rectal injection of the enzyme which he wished to immunise against. The first to immunise against rennin was apparently Morgenroth (31), whose success it was that induced Professor Dean to immunise against trypsin. Since 1900 a considerable amount of work has been done in immunising against other enzymes, such as pepsin, lactase, urease, tyrosinase and febrin ferment. Injection of these bodies into animals appears in fact to lead to the production of antagonistic bodies exactly in the same way as in immunisation against bacterial toxins or foreign

proteids. Von Dungern (32) has also shown that specific antibodies to bacterial enzymes could be demonstrated, especially to staphylococcal enzymes. In 1898 this observer demonstrated that the serum of a patient with osteo-myelitis was more than twenty times more inhibitory of the proteolytic enzymes of the organisms found in the diseased area than was normal serum.

(4) *Toxic products of autolysis.*—The by-products of anomalies of cell metabolism, however induced, may be themselves highly auto-intoxicative. This of course can only be if the normal protective mechanism against such toxic products be at fault. Of such auto-intoxicative products of morbid tissue activity the toxic bodies of fatigue, acute yellow atrophy, hepatic cirrhosis, abnormally active thyroids, phosphorus and chloroform poisoning, the leukæmias, pernicious anæmias, possibly diabetes, marasmus, extensive ulceration, absorption of exudates, traumatic changes induced by burns, and even of autolysing cancers, are all possible examples. If this be true of cellular disturbances not induced by bacteria, it may equally be true of cellular disturbances the direct result of bacterial invasion. A case in point is diphtheria. In this disease, as Sidney Martin points out (35), the toxæmic effects are probably as much due to secondary conversion of tissue proteids into poisonous albumoses by the diphtheritic poison as to direct intoxication by such.

Some of the products of self-digestion initiated by enzymes (non-bacterial) are unquestionably toxic, such as albumoses, peptones, etc. Experimentally, the chief toxic effects of injection of proteoses seem to be retardation of coagulation-time of the blood, arterial pressure fall, fever, and possibly some lymphagogue action (Heidenhain) (36). The appearance in the urine of proteoses when extensive tissue destruction is going on is suggestive. The same remark applies to albumosuria when any tissue or fluid is undergoing extensive autolysis; witness that condition occurring in acute yellow atrophy, phosphorus poisoning, resolving lobar pneumonia, breaking-down carcinomata, rapid lung destruction, absorption of inflammatory exudates, etc. Simon's work (37) on the injection of tuberculin is also highly suggestive. This observer found that by substituting injections of proteoses for tuberculin emulsions he was able to produce the rise of temperature characteristic of tuberculin reaction. It is not improbable that the products of autolysis set in motion by bacterial infection are partly responsible in other diseases besides diphtheria for phenomena generally ascribed directly to the bacterial factor only. If albumoses and peptones are toxic, the other cleavage product may well be so. Inasmuch as fever can follow aseptic suppuration, it is not unlikely that clinical signs such as rigors, fevers, etc., are frequently as much due to autolytic by-product absorption as bacterial. In autolysis of nerve tissue the toxic derivatives of lecithin were suggested in 1904 by Halliburton (39) as a cause of intoxication. Mott's work (40) on liberation of cholin from lecithin is also contributory to the same point. Another instance is the occurrence of systemic infection from breaking-down tumours. As a rule, constitutional signs in carcinomatous disease do not manifest themselves till breaking down is well marked, *i.e.* till autolysis is well established. The process of autolysis and of absorption of by-products of autolysis continues just the same even if bacterial contamination of a breaking-down surface carcinoma be eliminated. The degree of cachexia, indeed, is often quite proportionate to the amount of autolysis. If autolytic and other intra-cellular enzymes can, as appears to be the case, induce certain anomalies of their own cell-metabolism when the normal restraint keeping these in check is impaired, such aberration is not always necessarily due to bacterial invasion, even in diseases ostensibly bacterial. On the contrary, such disturbance, when autogenously produced, may well pave the way for bacterial infection. In other words, cellular anomalies may precede infection, as well as succeed. In this consideration may lie the key to the difficult problems of cryptogenic infection and latent persistency of infection. Autogenous morbid activity of cell-enzymes would then explain conversion of non-pathogenic bacteria into acutely pathogenic. Again, the products of such morbid activity may be not only auto-intoxicative, but also actually infective.

This has, in fact, been suggested by Professor Benjamin Moore (41) in the case of the exanthemata, where laborious search has failed to demonstrate a causal bacterial origin. In such a case the virus would certainly be ultra-microscopic, but by no means necessarily ultra-biochemical. Such questions can only be solved by extending research

along the lines of toxicity and infectivity of cellular products, which is, in fact, much needed. Professor Moore's arguments as regards the exanthemata are worth citing, because of their close bearing on the points I have raised :

(1) The incubation period would be that required for the production of the auto-catalyst in sufficient quantity to cause a general reaction with the tissue cells.

(2) The auto-catalyst, acting as the toxin of the disease, would increase up to the point of concentration of maximum effect. The cells at the same time would react as to ordinary toxin and produce the antitoxin, the efficient production of which would limit the disease.

(3) Variation in incubation periods of the same disease would be no argument against such a view, because the length of incubation would depend on the reaction of the cells affected. This consideration is much strengthened by the fact that in many cases of intoxication of purely bacterial origin the appearance of symptoms depends in no way upon any cycle of development of the parasites, but only on the reaction period of the cells.

(4) Variation in the immune body content of an individual would therefore depend—

(*a*) Upon the presence or absence in the blood of antibody capable of inhibiting at the outset the trace of auto-catalyst bearing the infection, and

(*b*) Upon the reactive power of the tissue-cells to the auto-catalyst or toxin.

(3) *Normal restraint of autolysis.*—Since apparently every tissue in the body can, under appropriate conditions, digest itself, the old vexed problem of how the living stomach protects itself against self-digestion becomes applicable to all organs and tissues. The suggestion that the reason why living tissue does not digest itself is because it is alive and not dead is only a re-statement of the original difficulty. There are, however, certain other suggestions which deserve mention. For instance, it has been expressly urged that intra-cellular enzymes do not digest the cells they belong to because they only exist there in pre-enzymic form—that is as zymogens. The apparent objection to this view—that if they do only exist as zymogens it is difficult to see how they carry out their normal metabolic functions—is disposed of by Wells (9). He suggests that they are only activated as need arrives, to be again inhibited when the need is temporarily past. Such suggestion involves, as he points out, a rhythmicality of function not unknown in metabolism. Weiner (10), on the other hand, has shown that an organ does not begin to autolyse until sufficient acid is produced by moribund cells to antagonise its alkalinity. Opie (11) has pointed out that two forms of autolytic ferments may be recognised in leucocytes—a peptic ferment acting only in acid media and a tryptic form only active in alkaline media. The tryptic ferment predominates in the polymorphonuclear leucocytes and the peptic in the lymphocytes. The presence or absence of the peptic as distinguished from the tryptic ferment furnishes a distinction between the lymphocytic pus of a tuberculous lesion and the polymorphonuclear pus of most pyogenic lesions. Another possible explanation of the absence of autolysis *in vivo* is that cell equilibrium is maintained during life in virtue of its food supply. Once this is interfered with equilibrium is disturbed and uncompensated autolysis begins. That this is an important contributory factor to intra-cellular restraint of autolysis there can be little doubt. Demonstration of bacterial autolysis when the organisms of typhoid and cholera are placed in distilled water or salt solution, the controls being planted in the ordinary media, is a case in point (12). In 1903 (13), Jacoby found that up to a certain point the autolytic enzymes of one organ are not autolytic to another—that is, he established a specificity.

The anti-tryptic index.—Quite early in the work on tissue autolysis note was taken of what is now a well-established fact. The blood-serum of man, monkeys, sheep, horses, and other animals was found to exhibit in marked degree a varying resistance to the action of autolytic enzymes. This resistance was found to disappear on heating, prolonged standing, and on the addition of dilute acids. The rate of autolysis *in vitro* was found to be markedly lessened if the autolysing organ was placed in fresh unheated horse-serum. The inhibitory body on which this resistant and protective body depends is effective against trypsin, and was therefore called anti-trypsin. Inasmuch, however, as it is also effective against pepsin and other secreted enzymes, and also against all tissue enzymes, except against an acid solution of HCl pepsin, which destroys it, a better name would be

anti-lysin, to denote its generic action. According to von Eisler (14) it is not specific in the sense of being more specific to auto-enzymes than to hetero-enzymes. Apparently it is less so. It seems to act not by destroying enzymes, but by inhibiting or paralysing their action. Weinland's observation of the protective power of anti-trypsin secreted by certain intestinal worms, as demonstrated by the absence of their digestion in active secretion, is familar. Delezenne (15) holds that the anti-tryptic action of normal serum is due to antikinase, a view contended by Bayliss and Starling (16), who maintain the direct action of anti-trypsin on the activated body. Cathcart (17) declares that the anti-trypsin of normal serum is attached to the albumen fraction of the serum, from which it cannot be detached even by prolonged washing, and not to the globulins. The anti-tryptic content of normal serum can, as I have elsewhere shown, be clinically demonstrated. If normal horse-serum, for example, be added to wounds or ulcers bathed in the strongly tryptic fluid of their own infected secretions, the tryptic action of the fluid is inhibited to such an extent that a wound treated in this way rapidly cleans (18). In favourable cases this is followed by rapid healing. By stripping one sample of normal serum of its globulins and adding to it the serum albumen content of another sample, it was found possible so to raise its total anti-trypsin content that the rise could be demonstrated both hæmatologically and clinically. This, in fact, is the basis of the preparation of the so-called anti-lytic serum which is now being extensively used in the treatment of gastric and duodenal ulcers (19).

In connection with the anti-tryptic content of normal serum, the following observations are of interest. Fluctuation, and therefore the site of most advanced softening in an abscess, is found in the centre of an abscess only, *i. e.* furthest away from the restraining influence of the anti-tryptic lymph-stream. The anti-tryptic content of lymph from a recent healthy wound is high, that of lymph from a wound showing no tendency to heal is, even in the absence of infection, low. An infarct undergoes central autolytic softening sooner than peripheral, no doubt for the same reason. The anti-tryptic power of infected pus is *nil.* In old exudates it is also less than in recent ones, and hence autolysis of the former proceeds more rapidly than does that of the latter. In lobular pneumonia is seen an excellent example of unrestrained autolysis. The contents of the alveoli, being removed from the inhibitory action of the lymph-stream, undergo rapid autolysis, whilst the cells of the alveoli, being constantly bathed in lymph with a high anti-tryptic content, escape.

The first observers to clearly demonstrate the anti-tryptic action of normal serum appear to have been Camus and Gley (20) in the year 1900. The first serious attempt to measure this action was made by Professor George Dean (21), who in 1901 published his paper on "Immunity in Relation to the Pancreas and its Ferments." The subject was extensively followed up in 1902 and 1904 by Glaessner, Cathcart, Levene (33), Stookey (33), Opie (34), and others (22). Professor Dean's method was to estimate the rate of digestion by trypsin of measured quantities of albumen, and the degree of inhibition of digestion by normal serum. He then adopted a method suggested by Fermi of estimating the inhibitory power of normal serum of digestion by trypsin of measured columns of gelatin. This method, with substitution of egg albumen for gelatin, now known as the method of Mette, was, as may be seen by reference to Dean's paper, independently elaborated by the latter. Methods of estimating the inhibition of tryptic digestion of albumen and gelatin in this manner are, however, of little practical value.

Various attempts were then made to estimate the anti-tryptic power of the blood serum in disease, though until 1908 without any considerable measure of success.

Most of the work previous to that date had been done by the method of Müller and Jochmann (23), which consists in the addition of varying quantities of serum, measured in loops of platinum wire, to a drop of pus in a Loeffler plate. The appearance or non-appearance of pitting after incubation was taken as a sign that the amount of inhibitory serum added had been insufficient to neutralise the pus ferment present. Such a method of estimation is obviously far too coarse to afford even an approximately accurate criterion of the anti-tryptic content of normal serum, and the earlier work of Hedin (24) had already shown that complete neutralisation could never be obtained. The contradictory results of the work of the authors of this method and their followers have in fact shown that it cannot be accorded serious consideration. The evaluation of ferment activity and, reciprocally, of the inhibitory power of serum, can only be determined by some method which allows the velocity reaction of the ferment to be measured. Hence the results obtained by the serum-plate method, or by the end-point methods of Cross, Bergmann and Meyer (25) are both contradictory and inaccurate. Estimation of the incoagulable nitrogen formed at different points in a tryptic digestion, and through this of the anti-tryptic content of an inhibiting serum, is impracticable because of the amount of serum required.

For these reasons, as Dr. Golla (26) has just shown, this observer has adopted the method of electro-conductivity of Henri (27), which has been recently elaborated by Bayliss. By this method Dr. Golla (28) states that he is able to gauge the relative anti-tryptic power of the blood with great accuracy, and in the course of his investigations he has discovered—

(1) That a rise of this anti-tryptic activity frequently takes place in tuberculosis.

(2) That such rise is often associated with a bad prognosis.

(3) That hetero-inoculation with tuberculin induces a rise of anti-tryptic activity in tuberculous subjects.

(4) That accurate determination of such rise affords a reliable guide to the efficacy of tuberculin injection, and that by this method it is possible to determine the point at which a dose of tuberculin should be exhibited.

Some of these observations I am able to confirm from my own clinique.

In twenty cases of tuberculosis a rise of the anti-tryptic index was found in all but one. The majority of these were pulmonary, the remainder, six in all, were renal, glandular, and peritoneal.

Of these twenty cases the only two that died had persistently high indices. Six when injected with tuberculin showed a further rise in an index already raised. In one of the cases referred to active disease was associated with a normal index. He subsequently did very well. To these observations I am able to add the following:

In cases where the guide afforded by a temperature chart, on the lines I have referred to, is absent, either from too small a variation of temperature or entire absence of such, it appears—

(*a*) That tuberculous patients with a high index react little, if at all, to artificial inoculation.

(*b*) That tuberculous patients with a low index show marked rise after similar stimulus.

A high index such as occurs in some cases with high fever, conforming to the type shown in Chart 26, is often associated with a bad prognosis. An index which was high when the temperature was raised in two cases approached, under artificial auto-inoculation, the normal when marked clinical improvement set in, and become actually normal when the temperature remained undisturbed, and when the disease was judged to be arrested. In one case the index did not again rise after tuberculin injection. In another case, with low index, response to inoculation was marked, and as the patient improved the response tended to diminish. In a third, who got progressively worse, the index was very high and tended to rise, whilst the response to inoculation was only comparatively slight, as evidenced by further rise of the index.

These observations, though at present incomplete, tend in some measure to confirm some of the views I have propounded, based on the variations in temperature that I have shown to follow auto-inoculation. In particular they support the contention that artificial inoculation of all kinds is contra-indicated in cases where intoxication without adequate reponse is great.

Apart from tuberculosis there is evidence, as the appended table shows, that variation can be demonstrated in such diverse conditions as carcinoma of breast, tongue, mouth, and cervix, rodent ulcer, acute septicæmia, leprosy and suppurative nephritis. In this table variation in the anti-tryptic content of the serum was found in twenty cases of tuberculosis of various organs, in four cases of syphilis, in two cases of rodent ulcer, in seven cases of carcinoma, in one case of acute septicæmia, in one case of suppurative nephritis, and in one severe case of leprosy. These serums were from cases in my own clinique or from such hospital cases as members of various hospitals were good enough to place at my disposal. The majority of the serum examinations were kindly undertaken for me by Dr. Golla.

It is also claimed by Brieger and Trebing (42) that they have been able to demonstrate variations in the index in cases of carcinoma, pernicious anæmia and nephritis. Variation in the anti-tryptic content of the serum in a case of lobar pneumonia was also demonstrated in 1903 by Ascoli and Bezzola (43).

Showing Presence or Absence of Variation from the Normal of the Anti-tryptic Index of various Serums.

	Source of case.	Nature of case.	No. of observations.
	Absence of Variation.		
1	Private	Healthy male	1
2	Lock Hospital (*a*)	Healthy male	1
3	Private	Healthy female	1
4	Private	Hydrocele of cord. (Otherwise healthy)	1
5	Private	Furunculosis. Male. (Otherwise healthy)	1
6	Private	Acne. Female. (Otherwise healthy)	1
7	Private	Varicose ulcer. Female. (Otherwise healthy)	1
8	Private	Floating kidney. Female. (Otherwise healthy)	1
9	Private	Cough, no physical signs	1
10	Private	Slight cough, no physical signs	1
		Presence of Variation.	
11	Private	Pulmonary tuberculosis. Female	4
12	Private	Pulmonary tuberculosis. Female	5

	Source of case.	Nature of case.	No. of observations.
13	Private . . .	Pulmonary tuberculosis. Male	4
14	Private . . .	Pulmonary tuberculosis. Male	6
15	Private . . .	Pulmonary tuberculosis. Male	3
16	Victoria Park Hospital (*b*)	Pulmonary tuberculosis. Female	1
17	Victoria Park Hospital (*b*)	Pulmonary tuberculosis. Female	1
18	Victoria Park Hospital (*b*)	Pulmonary tuberculosis. Male	1
19	Victoria Park Hospital (*b*)	Pulmonary tuberculosis. Male	1
20	Victoria Park Hospital (*b*)	Pulmonary tuberculosis	1
21	Victoria Park Hospital (*b*)	Pulmonary tuberculosis	1
22	Victoria Park Hospital (*b*)	Pulmonary tuberculosis	1
23	Victoria Park Hospital (*b*)	Pulmonary tuberculosis	2
24	Victoria Park Hospital (*b*)	Pulmonary tuberculosis	2
25	Private . . .	Renal tuberculosis. Female	1
26	Private . . .	Tuberculosis of cervical glands. Female	2
27	Private . . .	Probable tuberculosis, site unknown	4
28	Lincoln Hospital (*c*)	Tuberculous peritonitis. Female	2
29	Private . . .	Tuberculous peritonitis. Child	2
30	Private . . .	Tuberculous peritonitis. Child	2
31	Private (*d*) . .	Suppurative nephritis. Male	2
32	Private (*e*) . .	Acute septicæmia from ruptured ovarian cyst	2
33	Seamen's Hospital (*f*)	Leprosy	—
34	Lock Hospital (*a*) .	Syphilis	1
35	Lock Hospital (*a*) .	Syphilis	1
36	Lock Hospital (*a*) .	Syphilis	1
37	Lock Hospital (*a*) .	Syphilis	1
38	Cancer Hospital (*g*)	Rodent ulcer	1
39	Cancer Hospital (*g*)	Rodent ulcer	1
40	Cancer Hospital (*g*)	Carcinoma cervicis	1
41	Cancer Hospital (*g*)	Carcinoma mammæ	2
42	Cancer Hospital (*g*)	Carcinoma of throat	2
43	Cancer Hospital (*g*)	Carcinoma of scrotum	1
44	Cancer Hospital (*g*)	Carcinoma of tongue	2
45	Cancer Hospital (*g*)	Abdominal carcinoma	1
46	Cancer Hospital (*g*)	Carcinoma of mouth	1

(*a*) By the kindness of Mr. J. E. Lane.
(*b*) By the kindness of Sir Hugh Beevor.
(*c*) By the kindness of Dr. Daman, of Lincoln.
(*d*) By the kindness of Dr. F. A. Hort, of Nice.
(*e*) By the kindness of Mr. Lenthal Cheatle.
(*f*) By the kindness of Sir Malcolm Morris.
(*g*) By the kindness of Mr. Cecil H. Leaf.

In view of these facts it appears that marked variation from the normal may be as much a response to cellular changes in no way associated with bacterial invasion as to changes directly connected with such, as well as to bacterial infection without extensive cell change. That such aberrations of tissue metabolism as the index appears to indicate can be reflected in the blood-stream so as to be capable of ready measurement must be of profound significance.

As regards the interpretation to be placed on variation in the anti-tryptic index in disease little at present can be said.

For the purposes of this paper I am content for the moment to submit that its estimation cannot but have the highest value as a gauge of immunity response, because it appears to reflect, as I have shown, presence or absence of such response not only to bacteria and their products but also to the factors of morbid enzymic activity, and the toxic products of perverted cell change. The significance of such reflection in diseases such as carcinoma deserves serious study.

If such submission be sound, blood examinations exclusively directed to measurement of phagocytic activity and bacterial engulfment, however induced, can clearly, even if reliable, afford only a relatively insignificant gauge of immunity response as a whole.

To conclude as I began, I submit:

(1) That when Nature cures infection she converts tissues and bacteria into auto-inoculating agents, and thereby incites both cellular and bacterial restraint.

(2) That to provoke the last and ignore the first is too often to aim at half and expect the whole.

(3) That whenever practicable, auto-inoculation is the best method to employ when artificial aid is needed; and—

(4) That in thermometric charts and in measurements of the blood's inhibitory powers we have most useful guages of presence or absence of many kinds of stimulus and response.

Full conviction I can hardly hope to carry on the slender evidence here produced, but the attempt will not be fruitless if the attention of makers of modern medicine be for a moment diverted to issues other than the merely bacterial.

I wish to express my thanks to the following gentlemen, whose courtesy has enabled me to collect from their respective hospitals much of the clinical material that forms the groundwork of this paper: Mr. J. E. Lane, at the Lock Hospital; Sir Hugh Beevor, at the Victoria Park Chest Hospital; Mr. C. H. Leaf, at the Cancer Hospital; Sir Malcolm Morris, at the Seamen's Hospital; Mr. Lenthal Cheatle, at King's College Hospital; and Dr. Daman, at the Lincoln Hospital. I also wish to express my indebtedness to Dr. Rolleston and to Mr. Cheatle, for their great assistance in preparing this manuscript, and to Dr. Venning for continuous help in collection of the various serums referred to, and in many other ways, and in particular to Dr. Golla for his unfailing and generous help. Finally, I wish to convey my deep obligation to the anony-

mous philanthropist whose single-minded devotion to the highest aims of medical research has made this preliminary enquiry possible.

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Dr. D. LAWSON (Nordrach-on-Dee) said that if there was one indictment which the man in the street had brought against the medical profession which it had found difficult to answer it was the charge that they were liable to be carried away by one idea and to be blinded to all others which bore on the central point. There were many examples of that in the history of the treatment of tuberculosis in the last twenty-one years. There was the era of Koch, with his tuberculin, and in recent times Wright and his opsonic index. They were asked to discard all their clinical guides: the surgeon was asked to put on dark spectacles, because he need not now look at the appearance of a wound since he had, in the opsonic index, a sufficient guide for everything. Within the last six months several papers had appeared asking medical men to take up a fresh position and relinquish the opsonic index, taking in its place as a guide the temperature chart. Three years ago a paper was read in that room in which thirteen instances were brought forward to show that in cases where the temperature had been taken four-hourly and the opsonic index taken every day there was no direct relationship between the two. Not much had been heard of that since until Dr. Latham's recent paper, in which he came forward with certain evidence which seemed to point to the temperature and opsonic index bearing an inverse relationship to each other. Dr. Hort seemed to accept Dr. Latham's view on that point, and therefore he (Dr. Lawson) wished to ask if the author could explain three or four clinical points in that relationship. One found a certain type of tuberculosis which came into the sanatorium. Pulse and temperature were carefully taken, and often the temperature was found to be normal, but the pulse-rate ran anywhere between 90 and 120, extending over a period of weeks. That type of case, of which he had seen many in the last nine years, invariably went wrong, and if the pulse rate could not be brought nearer to the normal the patient died. In such a case the pulse was the guide, not the temperature, as to the advance of auto-intoxication. Secondly, there was the chronic fibroid type, in which the temperature was subnormal, and in which there might be a rapid pulse. There again the pulse was some guide, but the elevation of temperature was no guide. Thirdly, it had been said that a temperature reacting to exercises was presumptive evidence of the presence of that person's tuberculosis. If one set such a chronic fibroid case to walk half a mile it would cause a fall in the temperature, and everything showed there was increased auto-intoxication in that body; there was no rise of temperature to show that the supposed change had taken place. By living with cases and taking four-hourly temperatures every day, he was convinced that the temperature in itself was not a reliable guide as to the advance or retrocession of a lesion. He desired to protest against the recent trend to exalt temperature in cases of tuberculosis to the position of a fetish. He was sure that in a few years it would have slipped back to the position which it occupied before, and that clinicians in tuberculosis at least would return to the faith which experience had brought them to rely upon in the past, namely, the broad outline of the clinical facts.

Dr. F. PARKES WEBER said that among the various prophylactics against pulmonary tuberculosis (and some other diseases), one of the most generally recognised was the taking of muscular and respiratory exercise (not over-exercise) as a regular habit. Not only did exercise, especially open-air exercise, increase the resistance of the body towards infection, but when persons who took regular exercise chanced to become infected, the result of the exercise was by frequent auto-inoculation to stir up the resistance of the body towards the tuberculous focus before the latter had had time to become large. Thus, in persons who took regular exercise tuberculosis was resisted from the very commencement of the infection.

Dr. HORT, in reply, thanked the Fellows for listening so patiently to him.

April 26th, 1909.

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COMMON AFFECTIONS OF THE SKIN: THEIR EXACT DIAGNOSIS AND TREATMENT.*

By JAMES GALLOWAY, M.D., F.R.C.P.,
Physician to Charing Cross Hospital, and Physician to its Skin Department.

GENTLEMEN,—When your honorary secretary invited me to be present at this meeting of your Society and suggested the subject of my address, he left the responsibility of choosing the best plan of dealing with the matter on my shoulders. It soon was evident to me that the subject to be dealt with was a large one for discussion in the limited time at our disposal, so I decided that it would serve our purpose best if I selected some types of disease for consideration rather than to roam too widely over the large field open to me. May I ask you to accept this explanation as some apology for the fragmentary character of this address.

PYOGENIC AFFECTIONS OF THE SKIN.

Of the common diseases of the skin those produced by pus-forming micro-organisms may at first sight appear to be easily recognised, but clinical experience shows that their external appearances are apt to vary to so great an extent that exact diagnosis is not simple, and therefore appropriate treatment is not immediately used. In the case of children of school age these diseases are sufficiently common to cause public authorities to recognise that they are deserving of special treatment at the expense of the community, or, as it frequently turns out in such cases, at the expense of the medical profession. It is for this reason that the name "impetigo" appears as the generic name of pus-forming cutaneous disease of children, and is classed with ringworm, certain diseases of the eye, suppuration of the ear, and disease of the teeth by

* An Address to the Wimbledon District Medical Society.

the authorities in charge of the public schools as maladies for the cure of which they wish to invoke our philanthropic assistance.

Pathologists naturally incline to classify these skin diseases so far as is possible on the basis of the micro-organism producing the disease. Thus we hear of different types of impetigo, to be distinguished from certain varieties of suppurative folliculitis closely resembling them by the micro-organism presumed to be their exciting cause, but speaking from the clinical point of view these purulent diseases, excluding distinct affections such as boils and the different types of acne, are conveniently grouped together under the name of "impetigo." If, therefore, we use this term as expressing a sufficiently well defined clinical entity, the opinion widely accepted, though perhaps not conclusively proven, is that the primary lesion of the disease is due to the implantation and growth of a certain variety of streptococcus in the skin. The distinctive lesion produced by this organism is the raising of the upper layers of the epidermis by the exudation of a clear serous fluid, so that there is formed a vesicle or bulla. In a very short time after the formation of this initial lesion the pure characteristics are lost and the future course of the lesions and of the disease itself is due to a mixed infection, usually the yellow and the white pyogenic staphylococci being added to the original implantation of streptococci. The streptococci continue to be present, and the new lesions, which make their appearance often with great rapidity, are characterised in their turn by the formation of vesicles, bullæ, or by a raising or loosening of the epidermis, a feature which distinguishes the disease. The later formation of crusts, and perhaps more complicated forms of dermatitis, tends rapidly to obscure the initial lesions, but the clinical feature to grasp firmly is the raising of the epidermis in some form or other. It is scarcely to be doubted that many of the blistering eruptions hitherto classed under the name "pemphigus" are only variants of the type of infection under consideration.

The first variety of this type of disease to which I wish to draw attention is that affecting newly born children. Anyone who has had much experience in maternity practice among the poor, or in the out-patient department of a hospital where children are treated, or especially in a lying-in hospital, is aware that there occurs a peculiar skin disease in newly born infants characterised by the formation of vesicles or bullæ. It often occurs in epidemic outbursts, and is so fatal in its effects that it is still regarded as the plague of the children born in lying-in hospitals. The infants are apparently quite healthy at birth and at the onset of the disease. Within a few days of birth a small blister containing almost clear fluid is observed, usually near the umbilicus or on the lower part of the body. The lesion appears to be so harmless and the child continues to take food and to be so well that little apprehension is entertained by the nurse. Very soon after the first lesion a crop of these blisters shows itself spreading widely over the body, each one originating from a small reddened area of skin which ultimately forms its base. Probably a rise of body temperature is noted if the nurse is observant, and the child begins to lose condition. Treatment of the eruption is now commenced, and very difficult it is to devise treatment in a satisfactory manner, but in spite of rigid cleanliness and the most judicious antiseptic measures point after point of infection makes its appearance, till in the course of ten days or even a shorter time the surface is widely diseased, the child is reduced to a condition of serious marasmus, and it may be that deeper lesions of pyogenetic origin have made their appearance. The mortality among the children affected by this disease is very high. Various names are applied to this malady, usually chosen by observers who have had the opportunity and taken the trouble to make a study of the disease, but of these the term "*pemphigus neonatorum*" has perhaps made the greatest impression.

One of the chief difficulties lying in the way of reasonable treatment is the tendency to consider blistering eruptions among newly born children as due to inherited syphilis; and the first suggestion I would offer in the diagnosis of such cases is to take into consideration all other possibilities as to their origin before forming the diagnosis of syphilis. The recognition of these infantile bullous eruptions as being of pyogenetic origin is of great importance, and we should equally grasp the fact that the infantile syphilitic eruptions simulating them are rare. The diagnosis of inherited syphilis in such cases should be made only after careful consideration of the disease itself and the history of the case. Any scheme of treatment must deal with

the source of the infection. The disease has been conveyed to the child, and in consequence the mother and those attending the child must be scrutinised; in its turn the infected child is a source of infection—a point to be carefully borne in mind when, as is often the case, other newly born infants run the risk of infection. The infant itself, however, claims our first attention, and carefully devised antiseptic treatment must be used to the early lesions as soon as they are observed. The difficulty with which we have to contend is the extreme fragility of the patient. Strong antiseptic applications do more harm than good by causing damage to the neighbouring healthy skin and allowing of the re-inoculation of the disease on the injured spots. Lotions, ointments containing antiseptics, have the great drawback of macerating the healthy surface and thus again allowing of re-infection. The most reasonable plan for protecting the individual is by keeping the undamaged surfaces of the skin as dry as possible, and to save it from any sort of injury. Perfect clealiness of the underclothing and any dressings used must be observed. The lesions should be accurately and carefully disinfected, preferably by the medical man attending the case himself, using such antiseptics as weak solutions of the perchloride of mercury, saturated solution of boric acid, or the peroxide of hydrogen; the actual lesions themselves only should be thus treated. The neighbouring healthy surfaces should be repeatedly and carefully dusted with the finest dusting powders. These dusting powders should not contain starch, and are best prepared from the finer siliceous earths, advantageously mixed with zinc oxide and containing proportions of fine boric acid powder up to 50 per cent.

The ordinary forms of impetigo in children of school age produce lesions of so characteristic appearance that little difficulty in diagnosis is experienced, but there is a variety of the disease meriting a little special notice occurring in older children and adolescents, especially in boarding schools. In the case of the larger public schools it has become notorious under such names as "football impetigo," or, as it is often called, "scrum-pox" or "gravel-rash." This type of the disease is most common in schools where much Rugby football is played and often in the Rugby football teams. The infective material is spread from one player to the other during the game, or as the result of wearing infected jerseys, caps and other clothing, and no doubt also by carelessness in washing, by using towels already used by infected members of the team. Exactly the same type of lesion in the case of younger children characterises this form of the disease, the vesicating stage often being very readily noticeable. If these attacks produced only the milder form of eruption not much anxiety would arise, but in the case of these growing lads, during the period of adolesence, the tendency to eruptions of seborrhœic nature becomes developed, more markedly in the case of some individuals than in others. The attack of impetigo in these individuals with marked development of the "seborrhœic" state is occasionally of great severity. The pus infection spreads to the subcutaneous tissues, the lymphatic glands inflame, and severe cases of deep-seated and glandular suppuration are by no means uncommon. Medical men in charge of the public schools have had frequent experience of the almost epidemic prevalence of this exceedingly troublesome malady, and schools themselves have suffered as the result of outbreaks of this disease. This type of impetigo is therefore so well known amongst those who are likely to come into contact with it that little chance of failure in early diagnosis is likely. One of the most troublesome incidents in the history of the affection is that the disease may be imported into a school hitherto free by the contact of its Rugby fifteen with the members of an outside club some of whose members are infected.

The third variety of "impetigo" to which I would draw attention is the type seen in adults. In the case of the children of a family or of a community the disease is usually recognised, but in the case of the grown-up members, who may have left the locality in which infection arose, and are now in places where no present case of the disease is known, mistaken diagnosis is by no means uncommon. It is a frequent experience after the summer vacation to find grown-up persons of any age showing the disease, sometimes in a severe form. They say, and probably have been told by medical authority, that they are suffering from "eczema." Examination of the lesions soon discloses the fact that they are the true vesicating lesions of impetigo, and a little inquiry discloses the fact that the disease broke out some

what suddenly three or four weeks previously while on holiday, that they have been paying visits, and that the children of a house in which they lodged are known to have been affected by a similar disease of the skin.

In the two varieties of the disease I have mentioned last, careful antiseptic treatment of the affected surfaces rapidly produces a good result. The principle underlying the treatment in both cases is to do as little damage to the sound skin as is possible. The antiseptic remedies chosen should therefore be applied accurately to the affected areas, and all lotions and fomentations, except so far as is necessary for the purpose of removing crusts and purulent discharges, are inadvisable. The surrounding healthy skin should be kept dry, and should be most scrupulously dried after necessary ablutions. The mercurial antiseptics are the most efficient. In the cases referred to, in which the seborrhœic tendencies of the patient give rise to severe types of the disease, treatment by means of sulphur forms a very useful adjuvant to the mercurial antiseptic treatment.

"Seborrhœic Dermatitis" and "Eczema."

A second group of common diseases in which accuracy of diagnosis is the basis of efficient treatment is usually included in the wide category of eczema. Every observant physician is aware, although it is not so easy to provide an exact definition, of what is often called the seborrhœic type of skin. In the case of individuals who manifest this condition the symptoms are usually noticeable in early adolescence. The skin in early boyhood or girlhood is often said to have been of unusually fine texture, showing what may be compared to the appearance of "bloom" on the surface. At the age of twelve or thirteen years the fine texture of the surface and the delicacy of colouring begins to disappear, the surface assumes a "muddy" instead of a clear complexion, to the great disappointment of the parents, the hair loses its crispness in the case of girls, being difficult to arrange on account of its greasiness, and frequently pronounced pityriasis of the scalp develops. At the same time a tendency to inflammation of the skin-follicles is observed. The sweat and sebaceous glands seem to be unduly active, the orifices of the sebaceous glands become blocked with detached epithelium and inspissated secretion, the acini of the glands becoming gradually transformed into retention cysts. The epithelial plugs in the orifices of the glands are infested with micro-organisms; of these one species has ascribed to it the power of inducing the inflammation of the glands and surrounding structures, and giving rise to the troublesome and sometimes severely disfiguring lesions of acne vulgaris. In addition to this bacillus, it must be recollected that the ordinary pus-forming cocci are present. In such cases it is well known that superficial inflammations of the skin are common. Commencing as erythematous areas in positions such as the axilla, the groin, the pre-sternal and inter-scapular regions, and especially on the scalp, the affected regions soon become scaly, the horny epithelium which should be the natural protective covering of the skin is badly formed and desquamates, so that the clinical picture of a very characteristic superficial erythematous and scaly dermatitis is produced. This state of affairs is often described as "eczema"; with it may be the qualifying term *seborrhœic* eczema. If at this stage the injured surface becomes irritated by friction or scratching, or by the rapid growth of organisms already present, or it may be by the implantation of new strains of more virulent bacteria, then a new pathological picture characterised by erythema, œdema of the cutis, and the desquamation of rapidly growing and imperfectly formed horny epithelium is developed—not to be distinguished from other varieties of eczema. It is at this point that the error of diagnosis is likely to occur. The irritated seborrhœic dermatitis has actually passed into the condition of eczema, yet it is fundamentally the seborrhœic type of skin inflammation.

Treatment at this stage must necessarily be such as is adapted to the acuter forms of eczema, but in the earlier condition treatment of a totally different character would have controlled the seborrhœic state and prevented the development of the acute eczema which now faces the physician. The remedies suitable for the earlier stage are quite unsuited to the simple anti-phlogistic treatment now called for, if employed they will make matters much worse; on the other hand the simpler methods of treatment now required will have very little effect in getting rid of the morbid state which is the foundation of the disease. It is quite usual to find errors in treatment made in both directions. The prodromal condition is not recog-

nised as being a seborrhœic inflammation and is treated by remedies of a cooling and soothing character, while the later development is considered to be an outbreak of seborrhœic "dermatitis" and is treated by means of antiseptic remedies which inevitably aggravate the patient's unhappy plight. In dealing with the earlier simply "seborrhœic" inflammation the most efficient remedy at our disposal is sulphur, and the skill of the physician will be shown by the methods he employs in applying this remedy. It may very easily be abused and produce much irritation, and thus fail to give the patient the comfort and the satisfaction of seeing his disease vanishing; on the other hand it is frequently employed in ways which are quite inefficient. Individuals tolerate the remedy very differently. It may be employed as a powder to the surface, as an inunction in the form of ointment of various strengths and for various lengths of time, as a lotion, often very efficiently as a bath, and occasionally it can be prescribed with advantage internally. To obtain the good results and to acquire reasonable confidence in its use requires that form of skill which can only be acquired by observation and practice.

Lichen Planus—A Disease with Papular Lesions.

Of the less common diseases of the skin lichen planus gives rise to many errors of diagnosis. When it occurs as an outbreak of a few discrete papules scattered widely over the body it is apt not to be recognised; when it occurs as a widespread eruption of confluent papules it is often mistaken for psoriasis and the more chronic types of eczema; and again, when it occurs in the chronic, warty, "hypertrophic" form it once more fails to be recognised. Yet the disease is so comparatively frequent that a working knowledge of it should form part of every medical man's equipment. I recollect a well-known clinical teacher and valued friend of mine declaring that if a student could not recognise a straightforward case of lichen planus at the final examinations he deserved to fail. Judging by my experience at final examinations this ruling would prove to be of so severe a character as to be unworkable; nevertheless cases of this disease are, as a rule, easy of recognition. In the first mentioned discrete form it frequently gives rise to pruritus, and unless a careful inspection of the surface is made the very characteristic flattened polygonal papules fail to be observed. Even when casually noted they are considered to be the eruption of mild papular eczema, and the patient is not informed of its true character, and especially is not warned that the disease is likely to be of considerable duration. He is accordingly much disappointed with the results of treatment and very often wanders from doctor to doctor.

In the second type, characterised by confluent papules affecting larger areas, the error made is in mistaking the disease for a psoriasis-like eruption. Once more the patient is not informed of the long-lasting character of the lesions and disappointment ensues. Very frequently cases of the disease are considered by the doctor to be an unusual type of chronic eczema; he rests content with this diagnosis, and the possibility of its being lichen planus does not occur to him.

In the third variety, characterised by the hypertrophic type of lesion, the disease is very unlike the usual conception of the trouble; it is not flat, it is not red; it is, on the other hand, warty, frequently blackened, and exists for years, it may be, without giving rise to a great deal of trouble. The diagnosis is frequently missed altogether, or the eruption is put down as some chronic warty condition arising on the scar of an injury.

In all these cases the indication which will help most in diagnosis is the presence of the characteristic discrete lesions. As a rule they are not difficult to find. In the confluent or hypertrophic varieties there are usually a sufficient number of them to be seen round the margins of the confluent areas to allow of a firm diagnosis being made. There is one other diagnostic point of great value which should never be forgotten,—the disease affects the visible mucous membranes. If the buccal mucous membrane, therefore, is examined, the white, irregularly shaped, often streaked lesions may be seen on the inner surface of the lips, the inner side of the cheeks, on the palate, or on the tongue, and along with the cutaneous condition serve to complete the diagnosis. The lesions of lichen planus on the mucous membranes themselves, however, are not infrequently mistaken. Many cases of lichen planus of the buccal mucosa are thought to be, and are treated as, examples of syphilitic leukoplakia.

The treatment of lichen planus is unfortunately

not on such a sound foundation as is the case in the examples of disease I have already considered. The reason is not far to seek, for we are dealing with a chronic disease, the causation of which is quite unknown. Our methods therefore have to be entirely empirical, and such success as we may obtain is gained merely by gathering according to our knowledge the results of the experience of ourselves and of others. Yet much can be done on general lines to help our patients. In many cases those affected by the disease have little discomfort, except the mental want of ease resulting from the knowledge that they have this skin disease. Fortunately the majority bear this with a certain amount of philosophic resignation, but on the other hand there are others who not only suffer acutely from the pruritus that their malady is known to cause, but whose mental condition is so constituted that the disease and the irritation it produces becomes intolerable; they suffer from mental irritability, which gradually increases to such an extent that severe depression is produced, and some even approach the border-line of insanity. It is in such cases that the patience and skill of the physician will be taxed to the utmost to devise soothing remedies for his patient, and he will find before his patient is well that he has acquired a diversified experience of the use of emollient baths, of softening and anti-pruritic lotions, of the use of the more powerful anti-pruritic remedies, such as carbolic acid and perchloride of mercury, and it may be of general sedatives, and will have found out their good points and also their shortcomings.

Arsenic and mercury both possess value in the specific treatment of the disease, especially in its earlier and more acute stages. Arsenic has, however, been abused to such an extent in the treatment of skin diseases that its valuable properties are, for the time being, apt to be neglected. The trial from time to time of new preparations of the remedy and their reported success in the treatment of lichen planus serve to remind us that the remedy is of value. It should be used, when it is determined to employ it, with much care, and with the knowledge that its beneficial effects on this disease of the skin may not be experienced until distinct toxic effects of the drug become manifest, and the toxic effects of arsenic are of such a nature as not to be lightly evoked. Mercury is also of value in the eruptive stage of acute attacks. It should be used in small doses, and by the method preferred by the physician responsible, but for this particular purpose administration by the mouth should be recommended, and the preparation most suited is the liquor hydrargyri perchloridi. In the treatment of the chronic "warty" type of the disease recent experience shows that the use of X rays is of value. Cases of the disease which have long resisted resolvent treatment by means of salicylic acid and remedies of this group have been greatly benefited and even cured by the prudent and skilled use of this very elusive therapeutic measure.

Lessons from the Diagnosis of Syphilis.

The last two examples which I propose to take are from the field of syphilis, a disease well recognised as affording almost infinite variation in its manifestations, and an increasing variety in methods of treatment.

The first serves to illustrate the proneness of syphilis to excite other diseases to attack its victim and its habit of allying itself with the new invader. Syphilis, as it is seen in our population and among other peoples of about the same degree of civilisation, is especially a disease of young adults. We have already noted that another affection of the skin is apt to give trouble at the same period of life, namely, the eruptions due to seborrhœa. When a young person with seborrhœic tendencies is attacked by syphilis it often happens that the early period of the infection, when roseolar eruptions may be noted, is complicated by the rapid development of acute seborrhœic dermatitis. The patient comes for relief on account of severe eruptions of circinate seborrhœic inflammation affecting the groin, the lower part of the abdomen, the axillæ, and perhaps the face, and even among those with some experience of diseases of the skin the presence of syphilis is not suspected, the attention of the physician being distracted by the severe and wide-spread eruptions of seborrhœic character. It may be some weeks before the infiltrated papules, of unmistakably syphilitic origin, or the occurrence of lesions in the throat, or the development of condylomata, draw attention to the fact that our patient has syphilis and that this disease demands immediate treatment. Persons showing this unhappy combination of diseases frequently develop severe attacks of syphilis with inveterate cutaneous lesions; on the other hand, when the first acute onslaught of syphilis is dying away as the result of persevering and careful treatment, the hopes of the sufferer and of his doctor are disappointed by the outbreak of the severer, often follicular types, of seborrhœic disease.

Treatment in cases of this nature requires to be carried out with much prudence and care. Mercury is essential for the effectual treatment of the attack of syphilis but is often ill tolerated by these patients; while in the later stages the use of the iodides is almost certain to light up latent forms of seborrhœic folliculitis. Treatment by means of baths is greatly to be recommended in such cases.

Baths containing perchloride of mercury act in a very beneficial manner on the cutaneous lesions, and may be combined with the internal administration of the drug in the form which seems most desirable. Sulphur baths should also be given from time to time as a satisfactory plan of dealing with the complicating seborrhœic affections. Well-arranged treatment for syphilis at watering places where natural sulphur waters are available has much to be said in its favour for this class of syphilitic patient.

The second example illustrates how the appearance of an intercurrent skin affection, often due to the administration of drugs, may obscure the presence of syphilis and delay treatment. In such cases discriminating care and a good deal of experience may be required to arrive at the correct diagnosis. The drugs most likely to give rise to trouble are the bromides and, more commonly, the iodides. A patient may be brought suffering from a dangerous bullous eruption of evidently serious character. The contents of the bullæ may be hæmorrhagic, and the lesions themselves widely spread over the body, involving even the face and mouth. Possibly all likelihood of syphilitic infection is denied, or it may not be suspected. The physician exercises his ingenuity to find from what septic or toxic source his patient's dangerous malady may have arisen. He may suspect syphilis but finds his hands bound by the salutary rule that it is well to make a definite diagnosis of the disease before administering mercury, as the absence of the disease can never be affirmed after the course of mercury has been given, however circumstances may then indicate that the patient is free from syphilis. Under observation, however, the infiltrated eruption due to the formation of the syphilitic granuloma shows itself on some part of the body and the diagnosis of syphilis is firmly made. Then comes the information that the patient, suspecting that he or she may have acquired syphilis, has taken a course of Clarke's blood mixture or some similar nostrum containing iodides, and the eruption which has given rise to the early difficulty is pemphigus or hydroa due to iodine. The physician's attention has been distracted by this often apparently dangerous state, and he may have missed altogether the syphilitic disease from which the patient really suffers.

Difficulty and occasional error in diagnosis, leading, it may be, to serious error in treatment, is inevitable, but we should struggle to reduce these failures of our art to the smallest amount; and the aim of this paper is to remind us, even when harassed by professional duties, that it can only be by careful observation and some meditation that our inevitably accumulating experience can be rendered of value to our patients, ourselves, and perhaps to our brethren.

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SOME CLINICAL ASPECTS OF PERNICIOUS ANÆMIA.*

By HERBERT FRENCH, M.D.Oxon., F.R.C.P.Lond.,

Assistant Physician to Guy's Hospital; Pathologist and Lecturer on Forensic Medicine at Guy's Hospital; Late Radcliffe Fellow of Oxford University.

GENTLEMEN, — I have recently had occasion to read through the records of the cases of pernicious anæmia that have been in Guy's Hospital since 1890, and your secretary has asked me to say a few words about them from the purely clinical point of view. The main features of the disease are so well known that I need not refer to some of them at all; indeed, I propose to restrict my remarks to seven particular points, namely, the following:

(1) The temperature charts of pernicious anæmia cases.

(2) Pigmentation of the buccal mucosa in pernicious anæmia.

(3) The size of the spleen in pernicious anæmia.

(4) The nerve symptoms in pernicious anæmia.

(5) The variability in the colour index in pernicious anæmia.

(6) The injustice of the epithet "pernicious" in some of the cases.

(7) The difficulty frequently met with in accurately dating the beginning of the illness, with some thoughts that this difficulty suggests.

Before proceeding to discuss each of these points in turn I should like to say that my present use of the term "pernicious anæmia" is a decidedly restricted one; some remarks that I shall make at the end of this paper will indicate that I think the limitations may some day be shown to need relaxation, but meanwhile I do not include as pernicious anæmia any case that has not at one time or another exhibited oligocythæmia with a high colour index and no leucocytosis during life, and should death occur, a definite Prussian blue reaction in the liver. Fifty-eight such cases passed through the wards of Guy's Hospital between the years 1890 and 1907. The cases previous to 1890 have been collected together and published in the Guy's

* Delivered before the Medical Society of London.

Hospital Reports in papers by Dr. Pye Smith, Dr. Frederick Taylor, and Dr. Hale White.

I must ask your indulgence if you do not find the following remarks in any way new or original. They will perhaps serve to bring out a few clinical points upon which I think less stress is sometimes laid than should be, and I hope they will elicit a discussion.

(1) The Temperature Charts of Pernicious Anæmia Cases.

(Oral temperatures.)

First let me refer to the temperature charts of pernicious anæmia cases. It is remarkable how constantly there is slight pyrexia. I have copied out the charts in all the cases I have been able to find, and three points about them stand out saliently, viz. first, that when the patient is ill enough to be admitted to hospital it very seldom happens that there is not a rise to something between 99° and 100° F. every evening; secondly, that pyrexia exceeding 101° F. is possible in pernicious anæmia, though decidedly unusual unless there is some intercurrent malady such as tonsillitis or pneumonia; and thirdly, that there is little tendency to subnormal temperatures in the morning, especially if the records are made only at 10 a.m. and 6 p.m.

Judging from what happens in other asthenic conditions, such as those associated with chronic heart disease for example, one would not have been surprised if the temperature in a severe case of pernicious anæmia had shown a tendency to be persistently subnormal; judging from what happens in cases of chronic sepsis on the other hand, one might have expected a moderate degree of evening rise, but at the same time a considerable drop below normal in the morning. Neither of these types of temperature chart is at all like that of most cases of pernicious anæmia, however; in this disease it may be roughly said that the more the general condition of the patient improves under treatment the less does the tendency to evening pyrexia become; but that when the patient is decidedly anæmic and ill the condition is not like that of the great majority of pernicious anæmia cases, unless the patient's temperature tends to rise to something between 99° and 100·5° F. every evening without any great fall below normal at 10 a.m. in the morning. Chart after chart taken from successive cases of pernicious anæmia shows this slight but persistent pyrexia. The smallness of the variation in temperature at different times of the day in some cases is well exemplified by the case of Louisa W—. The notes of her condition are as follows:

Louisa W—, æt. 43 years, a florist, was admitted under the care of Dr. Taylor, on December 19th, 1903, and died on February 13th, 1904. She came in for weakness and vomiting. She stated that she had never been ill until six months previously, when rapidly increasing weakness compelled her to give up her work. She also suffered from pains in the epigastric region and from vomiting, especially after taking food. There had been a moderate degree of epistaxis on several occasions. The catamenia had been regular, but latterly the loss of blood had been considerable each time. The patient was so weak that she could not walk three steps without resting; at the same time she was not emaciated.

The liver was palpable, smooth and decidedly tender; the spleen was palpable two and a half inches below the costal margin. The cardiac impulse was in its normal position, but there was a loud hæmic bruit in the pulmonary area. The teeth were in particularly good order and the mouth was clean. The nervous system appeared to be natural. There were decided hæmorrhoids and they bled considerably each day. Indeed, the first diagnosis made in the case was that the anæmia was secondary to hæmorrhage from the piles. The blood-counts and the post-mortem findings, however, indicated pernicious anæmia. The pulse-rate varied from 88 to 108, the respiration-rate from 20 to 32. The temperature chart showed a typical evening rise to about 100° F. The urine had a specific gravity of 1010; on one occasion only did it contain albumen; there was no hæmaturia; uric acid crystals were deposited spontaneously, urobilin was not mentioned.

Arsenical treatment was tried, but there was great difficulty in continuing it owing to vomiting and diarrhœa, both of which became very severe before death. The latter came about by exhaustion.

The chief points noted at the post-mortem examination were: that the lungs were healthy; the heart presented much sub-pericardial fat, with obvious tabby-cat striation in the muscle, par-

ticularly in the musculi papillares of the left ventricle. The liver was large and pale and gave an even more marked Prussian blue reaction than usual. The spleen was moderately enlarged and gave a fairly good blue reaction, less in degree than that in the liver. The kidneys were pallid and one of them was scarred from former infarcts; they were not tested for Prussian blue reaction.

The blood-counts made during life were as follows:

Date.	Red corpuscles per c.mm. (Thoma-Leitz).	Red corpuscles per cent of normal.	Hæmoglobin per cent. of normal (Haldane).	Colour index.	Leucocytes per c.mm. (Thoma-Leitz).
Dec. 20, 1903	2,050,000	41	35	0·853	8000
Jan. 5, 1904 .	1,339,000	27	25	0·926	—
Feb. 2, 1904 .	787,500	16	24	1·500	6532

A differential leucocyte count in December, 1903, showed:

	Per cent.
Small lymphocytes . .	27·2
Large „ . .	2·4
Polymorphonuclear cells .	66·6
Coarsely granular eosinophile cells .	3·8

For nearly seven weeks her temperature never touched normal once.

So marked a pyrexia might readily lead to difficulties in diagnosis. For example: If diarrhœa were a prominent symptom and the spleen were palpable, as is often the case in pernicious anæmia, typhoid fever might easily he simulated, and in more cases than one pernicious anæmia patients have given the history that their illness resulted directly from an attack of something obscure that was regarded as typhoid fever. It may well be that the supposed typhoid fever in some such cases was really the pernicious anæmia itself with its pyrexia. A case in point will be referred to presently.

Another four-hourly chart from a pernicious anæmia case (Hannah H—), exhibited a more remittent type of temperature; it is also an example of the way in which the slight evening rise gradually dwindles off and finally ceases as the patient's blood condition and general health improve. She was a typical case of pernicious anæmia.

Hannah H—, æt. 31 years, a housewife, was admitted under the care of Dr. Hale White on October 1st, 1903, for general weakness and for loss of weight of six months' and for vomiting and nausea of three months' duration.

She stated that for two years past she had been dyspeptic, and that six months ago, without apparent cause, she began to ail. Her menses became scantier each month and she gradually became weak. She suffered from alternate anorexia and bulimia. Headaches and noises in her head came on, and palpitations on the slightest exertion. Latterly there had been bleeding *per anum*, oozing of blood from the gums, and streaks of blood in the vomit.

The teeth were much decayed. The face was extremely pallid, and dirty white rather than lemon-yellow. The heart presented hæmic bruits and a canter rhythm, though the impulse was in its normal position. The abdomen was thin enough for the liver to be *seen* one and a half inches below the ribs. The spleen was just palpable. The urine contained indican in excess but no obvious urobilin.

Asenical treatment was adopted, but it was difficult to maintain on account of severe attacks of very foul diarrhœa. Various diagnoses were suggested, but that of pernicious anæmia was made obvious by the blood-counts, which are given below.

In this patient both knee-jerks were extremely brisk, and there was ankle clonus in one foot but not in the other.

The retinæ were natural. The temperature was often 101° F. each night at first, and then as improvement took place it only rose to 100° F. and later to less still.

She was discharged very much improved in health on December 10th, 1903, and she remained comparatively well for two months. She then began to lose ground again, the menses decreasing as before, weakness and palpitations increasing, the phlegm becoming streaked with blood, and vomiting taking place after food. She was re-admitted under Dr. Taylor on June 20th, 1904, and re-discharged, again relieved, on July 23rd, 1904. She was extremely pallid on admission, with tenderness of the shafts of the long bones. The liver was felt two and a half inches below the ribs; the spleen was not felt this time. There was

pyrexia as before; the lung signs were natural; the heart was of normal size but presented hæmic bruits in all areas, and there was a *bruit de diable* in the neck.

The urine had a specific gravity of 1015 and it contained neither albumen nor blood.

Arsenical treatment led to troublesome diarrhœa, but at the same time the patient's general condition greatly improved.

Upon inquiry at her old address it was learned, on August 15th, 1907, that "Mrs. Hannah H— has been dead for over twelve months now," so apparently she survived her second rally for a year or more.

The following were the blood-counts in her case:

Date.	Red corpuscles per c.mm. (Thoma-Leitz)	Red corpuscles per cent. of normal	Hæmoglobin per cent. of normal (Haldane).	Colour index.	Leucocytes per c.mm. (Thoma-Leitz).
1903					
Oct. 1	987,000	19	29	1·526	5000
,, 4	750,000	15	25	1·666	—
,, 7	650,000	13	25	1·923	—
,, 18	700,000	14	28	2·000	5000
,, 25	900,000	18	28	1·555	—
Nov. 1	1,100,000	22	39	1·776	—
,, 8	1,100,000	22	35	1·591	—
,, 14	1,400,000	28	39	1·393	—
,, 20	2,500,000	50	60	1·200	—
,, 29	2,500,000	50	60	1·200	—
1904					
June 22	868,750	17	26	1·529	7187
July 8	2,500,000	15	58	1·160	—

Notes.—On October 1st, 1903, many poikilocytes and megalocytes were present in films, and nucleated red cells to the extent of one to every sixty leucocytes.

On October 18th, 1903, the differential leucocyte count was "practically normal."

On June 24th, 1904, poikilocytes and megalocytes were numerous, and nucleated red cells were seen.

Differential Leucocyte Count.

	June 22, 1904. Per cent.	July 8, 1904. Per cent.
Small lymphocytes	54	20
Large ,,	6	12
Polymorphonuclear cells	38·5	60
Coarsely granular eosinophile cells	1·5	8

Two more charts will be sufficient, I think, to emphasise my point. One, from the case of Edward B—, æt. 53 years, is a very good example of what I should call the persistent slight evening pyrexia of pernicious anæmia. The other one, from a fatal case, Samuel D—, æt. 45 years, shows the increasing pyrexia towards the end of the disease and a final drop to normal or below it just before death.

Edward B—, æt. 56 years, was admitted under the care of Dr. Goodhart on May 24th, 1893. He became relieved and was discharged on July 22nd, 1893; he relapsed soon after, was re-admitted on November 28th, 1893, and died on June 9th, 1894.

He gave the history that he was quite well until five years before his first admission, and that he then suffered a bad attack of diarrhœa during the summer, losing much blood *per rectum* at the time. Each summer since then he had had a precisely similar and very severe attack, lasting some weeks each time. In March, 1892, he first thought he was "jaundiced" and told his doctor so. In July, 1892, he was so much worse that he lay up in Croydon Hospital for twenty-two weeks. After that he worked for eight weeks, but became progressively weaker and more ill. He had suffered from pains in the chest and abdomen and from giddiness for over two years; these, together with prostrating weakness, were his main symptoms on admission.

He was the typical colour. There had only been slight loss of bulk, and he weighed 11 st. 1 lb. without clothes.

His temperature was always at least 99° F. at night; often it was 100° F., and sometimes 101° F.

There were well-marked retinal hæmorrhages and hæmic bruits. There had been œdema of the ankles, but this went when he lay in bed. Appetite was poor but there was no vomiting. The spleen was not palpable at first but ultimately it became quite large. The liver was felt down to the level of the umbilicus or lower. The urine had a specific gravity of 1010; it was constantly pale; it deposited uric acid crystals spontaneously. It was free from albumen except on one occasion, and from blood; it gave no urobilin band to the ordinary spectroscopic test. Epistaxis occurred spontaneously more than once, and at one time there were subcutaneous petechiæ upon the arms and diffuse purpuric blotches on the legs.

After the administration of arsenic there were one or two diarrhœic attacks, but there had been none before arsenic was given.

Itching of the skin was at one period a very troublesome symptom, though jaundice was entirely absent.

During the final relapse the patient became œdematous, and serous exudations occurred. Finally there was increased pyrexia with rigors due to a terminal infective endocarditis, which was the immediate cause of death.

The post-mortem examination showed a well-nourished body, profoundly anæmic but with very bright yellow-coloured fat. There was some œdema of the nether limbs. Each pleural cavity contained about three pints of serous fluid, the pericardium about eighteen ounces of a similar fluid, and the peritoneum forty-one ounces. The lungs were very pale and extremely œdematous. The alimentary canal looked normal. The heart was pallid, and the mitral and pulmonary valves œdematous, the former being incompetent and the latter bearing small recent granulations all along it near its free edge. The spleen weighed nineteen ounces and was dark and tough. The kidneys weighed thirteen ounces, and the liver eighty ounces. Liver, spleen, and kidneys all contained a large excess of iron and gave a well-marked Prussian blue reaction.

The blood-counts made during life were as follows:

Date.	Red corpuscles per c mm.	Red corpuscles per cent. of normal.	Hæmoglobin per cent. of normal.	Colour index.
1893				
May 24	800,000	16	30	1·875
June 5	1,250,000	25	35	1·400
,, 20	2,100,000	42	50	1·190
July 7	1,850,000	37	45	1·216
,, 21	2,750,000	55	60	1·091
1894				
Jan. 15	500,000	10	18	1·800
,, 28	1,150,000	23	—	—
Feb. 6	900,000	18	20	1·111
Mar. 7	1,000,000	20	20	1·000
,, 22	900,000	18	18	1·000
Apr. 10	1,250,000	25	20	0·800
May 4	1,600,000	32	15	0·469
,, 29	2,000,000	40	30	0·750
June 8	1,850,000	37	19	0·512

Note.—There was no leucocytosis, and films were typical of pernicious anæmia.

Samuel D—, æt. 45 years, was admitted under the care of Dr. Hale White on December 23rd, 1893, and died on February 9th, 1894.

He gave a history of having been dangerously ill six years previously with symptoms which were diagnosed as "cholera," though he had never been abroad. He recovered after some while and enjoyed fair health on and off for five years. He then began to get progressively weaker, to lose his appetite, to suffer from very troublesome diarrhœa, and from breathlessness on ordinary exertion. He had been continuously under medical treatment from August, 1893. His height was 5 ft. 5 in. and his weight 8 st. without clothes.

His skin had the primrose yellow colour of pernicious anæmia. There were hæmic bruits in the mitral, aortic and pulmonary areas and in the neck. Neither liver nor spleen could be felt. The urine was dark and contained both indican and urobilin, but neither albumen, blood, nor sugar. The optic discs and retinæ were at first natural, but later they developed hæmorrhages.

Much diarrhœa interfered with arsenical treatment. There was a very slight improvement for a time, then a relapse, and the patient lay semi-comatose for some days before he died. There was no œdema. The lungs and pleuræ were natural except for old adhesions over the latter and for petechial hæmorrhages both beneath the pleuræ and in the substance of the lungs. The heart weighed 12 oz.; the valves were natural, but the muscle exhibited tabby-cat striation.

The stomach and intestines all looked quite normal; there were not even any enlarged follicles in the colon. The liver was pale brown and gave a fairly good Prussian blue reaction with the potassium ferrocyanide and hydrochloric acid test. The spleen weighed 7 oz. and was firm and dark. The kidneys together weighed 9 oz., and they were pallid but otherwise natural.

The blood-counts during life were as follows:

Date.	Red corpuscles per c.mm. (Thoma-Zeiss).	Red corpuscles per cent. of normal.	Hæmoglobin per cent. of normal (Oliver).	Colour index.
Dec. 24, 1893	1,000,000	20	17	0·850
Jan. 1, 1894	1,200,000	24	20	0·833
Jan. 19, 1894	1,450,000	29	24	0·827
Jan. 26, 1894	850,000	17	25	1·470

There are doubtless cases of pernicious anæmia in which there is no such slight evening pyrexia, but I would submit that this is when the patients have rallied and have improved considerably in health.

Pyrexia in pernicious anæmia has been recorded again and again, of course, but I do not think that enough stress has been laid, as a rule, upon the fact that in nearly every case of the disease in which the patient is moderately or severely ill there is a slight but definite and often long continued evening rise to somewhere between 99° F. and 100° F., or even 101° F.

(2) Pigmentation of the Buccal Mucosa in Pernicious Anæmia.

In the next place I should like to recall to memory the remarks made by Dr. Hale White before the first meeting of the Association of Physicians of Great Britain and Ireland, upon a case of pernicious anæmia in which there were abnormal pigmentary deposits, not only in the skin but also in the buccal mucosa. It is well known that Addison's disease and pernicious anæmia may present such similar symptoms that it is sometimes difficult to be sure which malady the patient is suffering from. It was formerly a generally accepted opinion that the presence of pigmentary deposits beneath the buccal mucosa inside the lips or cheeks would be decisive in favour of Addison's disease in such a case. Unfortunately this can no longer be maintained, for in the two following cases of pernicious anæmia, in which the diagnosis was confirmed by post-mortem examination at which the supra-renal glands were normal to the naked eye, there was well-marked pigmentation of the buccal mucosa. The first of them was the one in which Dr. Hale White himself observed the phenomenon; the other is a hitherto unpublished case.

Frederick V—, æt. 33 years, a shoemaker, first came under Dr. Hale White's care in 1904, and was in the hospital from August 2nd to December 15th. There was a long and indefinite history of increasing weakness and unfitness for work, and upon examination the chief point that attracted attention was the colour of the skin. The man was not emaciated, though tall and spare; the lips were pale, but the skin, instead of being primrose or lemon-yellow was an unhealthy sallow tint, and upon closer inspection it became clear that there was an abnormal pigmentation in it, partly diffuse and partly in small localised dark brown freckle-like spots over the body. Addison's disease at once suggested itself as a diagnosis, and at first sight this seemed to be confirmed by the presence of well-marked sepia-coloured pigmented areas and streaks within the mouth, particularly on the inner aspect of the cheeks, precisely as in Addison's disease. The difficulty was rendered greater, perhaps, by the variations in the colour index of the blood, which was sometimes low and sometimes high. Dr. Hale White adhered to the diagnosis of pernicious anæmia, laying much more stress on the high colour indices than upon the low ones.

Arsenical treatment was adopted, but without great relief, and later supra-renal extract, iron, and bone-marrow were all tried. The patient went out a little better than when he came in, but was twice re-admitted in 1905. He rallied again and lingered on till 1907, when he finally died, and the post-mortem examination showed that pernicious anæmia was the correct dignosis and not Addison's disease.

The blood-counts during life were as follows:

Date.	Red corpuscles per c.mm. (Thoma-Leitz).	Red corpuscles per cent. of normal.	Hæmoglobin per cent. of normal (Haldane).	Colour index.	Leucocytes per c.mm.
1904					
Aug. 5	2,100,000	42	44	1·048	2400
Sept. 3	2,260,000	45	36	0·800	—
,, 6	2,470,000	49	34	0·694	3125
Oct. 3	1,450,000	29	37	1·276	2656
,, 14	2,060,000	41	34	0·829	2188
,, 20	1,350,000	27	34	1·259	2810
,, 28	1,760,000	35	35	1·000	2030
Nov. 12	1,650,000	33	36	1·091	1800
,, 20	1,650,000	33	36	1·091	2500
Dec. 10	2,200,000	44	37	0·841	2000
1905					
Jan. 20	1,731,250	35	36	1·029	—
Feb. 3	1,350,000	27	27	1·000	1250
Dec. 2	1,750,000	35	45	1·286	1800
,, 14	1,750,000	35	26	0·743	4375

In this case both plantar reflexes were persistently extensor, though there was no ankle clonus and no increase in knee-jerks. There was also paræsthesia of the legs to electrical stimulation, the strongest shocks being scarcely felt though other sensations seemed natural.

On February 3rd, 1905, seven nucleated red

cells seen in counting one hundred white cells. February 3rd, 1905, differential leucocyte count:

Small lymphocytes	68 per cent.
Large „	2 „
Polymorphonuclear cells	27 „
Eosinophile cells	3 „

The other case was as follows:

Annie B—, æt. 33 years, a housewife, had been in St. Thomas's Hospital from November, 1905, to January, 1906; she then came into Guy's Hospital under the care of Dr. Taylor, from May 19th, 1906, to August 3rd, 1906, when she was discharged relieved, only to relapse at once and be re-admitted to St. Thomas's Hospital in September, 1906, dying there in November, 1906.

She was a married woman who had had one child and no miscarriage. Her illness started eight months before her first admission to St. Thomas's Hospital with an increasing general weakness. She had also noticed puffiness of her ankles and feet, especially on walking, loss of appetite, dyspepsia, and a ringing in her ears.

On admission she was a typical case of pernicious anæmia. The heart was a little dilated and there were generalised hæmic bruits and a *bruit de diable* in the neck. The liver came one and a half inches below the ribs in the right nipple line. The spleen was not felt. There were no retinal hæmorrhages. There was widespread pigmentation of the skin both in specks and spots and in bigger patches, in addition to which there was *decided pigmentation in or beneath the buccal mucosa on the inner aspects of the cheeks.* This was confirmed at autopsy.

The pigmentation was not known to have antedated arsenical treatment. The urine was high coloured, of specific gravity 1012; it contained neither albumen nor blood, but gave a well-marked urobilin band spectroscopically. The patient's temperature was often 99° F. to 100° F. The pulse-rate was 88 to 100 and the respiration-rate 20 to 24. There were curious subjective sensations of paræsthesia, particularly in her thighs, which seemed to her at all times to feel "too hot inside and too cold out," in a way which struck her as being both abnormal, inconvenient, and different to her sensations in other parts of the body and limbs.

The behaviour of the knee-jerks is noteworthy. They were present on admission to St. Thomas's Hospital, but they had disappeared on December 21st, 1905, when liquor arsenicalis was being given in 9-minim doses. The medicine was stopped and the knee-jerks had returned on December 27th. Liquor arsenicalis in 3-minim doses was again given and the knee-jerks were again absent on January 3rd, 1906. They had returned by the time of her admission to Guy's Hospital in May. They were again absent in September, 1906.

Toward the end pleurisy set in on the right side. and on November 11th, 1906, three pints of pleuritic fluid were withdrawn, followed on November 25th by another four pints. The patient collapsed, and died after the second aspiration.

Post-mortem, prominent inflammation of the alveolar sockets with looseness of all the teeth were noted, also pigmentation of the inner aspect of the cheeks. There were shallow circular ulcers of the skin around the left patella. Acute pleurisy had occurred on both sides. The heart was not dilated; it was encased in the usual bright yellow fat; its valves were healthy, its muscle pale and soft. The liver was large and paler than normal and gave a good Prussian blue reaction. The kidneys were markedly anæmic and gave a slight Prussian blue reaction. The spleen was large, and pale red, and gave some degree of Prussian blue reaction. The marrow of the long bones was red. All the other structures and organs, except for pallor, looked natural.

Blood-counts during life were as follows:

Date.	Red corpuscles per c.mm. (Thoma-Leitz).	Red corpuscles per cent. of normal.	Hæmoglobin per cent. of normal (Haldane).	Colour index.
1905				
Nov. 18	981,250	19	25	1·316
„ 30	843,750	19	20	1·052
Dec. 12	1,100,000	22	25	1·136
„ 30	2,231,250	45	40	0·888
1906				
Jan. 4	3,325,000	66	50	0·757
May 20	1,800,000	36	40	1·111
June 8	2,000,000	40	25	0·625
„ 19	2,040,000	41	35	0·854
„ 29	2,640,000	53	40	0·755
July 20	3,800,000	76	—	—
Oct. 5	679,687	13	20	1·539
„ 18	1,178,125	23	25	1·087
Nov. 11	1,259,400	25	25	1·000

On many occasions typical poikilocytosis and megalocytosis were observed and many nucleated red cells. There was no leucocytosis.

Microscopically the marrow showed well-marked

megaloblastic change. The heart exhibited pigmentary degeneration, fatty change, and slight mononuclear infiltration. The iron granules in the liver-cells were chiefly at the periphery of the lobules. The spleen showed no fibrosis. The kidneys exhibited catarrhal changes in the tubules and also iron granules in the epithelial cells.

For some of the notes of this case I am much indebted to Dr. H. C. Squires.

It may well be asked what *rôle* arsenic plays in the occurrence of this intra-buccal pigmentation in pernicious anæmia. I am unable to answer this question absolutely, but I think I am right in saying that in the Manchester epidemic of arsenical poisoning such pigmentation within the mouth was not observed. Moreover, it is known that pathological pigmentation of the skin may occur in pernicious anæmia even when no arsenic has been given. Nevertheless, arsenic had been employed in the treatment of both the above cases, and therefore, although I can say that pigmentation of the buccal mucosa can occur in pernicious anæmia cases treated by arsenic, I am unable to say whether similar pigmentation can occur in pernicious anæmia cases in which no arsenic has been used.

I may perhaps add that the appearance of the buccal pigment is precisely similar to that seen in Addison's disease.

(3) The Size of the Spleen in Pernicious Anæmia.

Passing next to a consideration of the size of the spleen in pernicious anæmia, I think it worth recording that although the general statement that the spleen is not enlarged may be true as a rule, nevertheless there are quite a number of cases in which the spleen is large enough to be readily palpated without any special expertness on the part of the observer. Clinically, out of fifty-six consecutive cases there were eighteen in which the spleen was felt with ease. I would compare the degree of enlargement in these eighteen with that which occurs in typhoid fever; in the greater number the spleen came below the costal margin for something between half an inch and two inches; in a few, however, the enlargement was greater, the spleen reaching down to below the level of the umbilicus in one. I need not burden you with the clinical details of these eighteen cases, beyond, perhaps, mentioning that in nine of them the liver was not palpable at the same time as the spleen, whilst in the other nine it was.

It is of importance to add, however, that the clinical observation of splenic enlargement in so considerable a proportion of pernicious anæmia cases is quite borne out by the results of post-mortem examinations.

The actual weights of the spleens are known for fourteen out of the total fifty-eight cases, and they vary from $3\frac{1}{2}$ oz. or 105 grm. on the one hand to 26 oz. or 746 grm. on the the other. Eleven out of the thirteen weighed more than normal, and it is noteworthy that six out of the thirteen weighed no less than 10 oz. or more. The existence of a spleen that can be readily palpated is, therefore, by no means unlikely in pernicious anæmia.

Weight of Spleen in Thirteen Consecutive Fatal Cases of Pernicious Anæmia.

(Normal weight 5 ozs., or 140 grms.)

Case.	Ounces.	Grammes.
1	$3\frac{1}{2}$	105
2	4	113
3	$6\frac{1}{3}$	181
4	7	198
5	$7\frac{1}{4}$	207
6	$8\frac{1}{8}$	248
7	$8\frac{3}{4}$	255
8	10	283
9	$10\frac{1}{2}$	306
10	12	341
11	14	397
12	19	539
13	26	746

I am sure that the observations of many of you here will confirm this, and yet I think that it is a point that too little stress is laid upon as a rule. The fact that pernicious anæmia may be a cause for definite enlargement of the spleen clearly increases the number of other conditions with which under certain circumstances it might become confused.

(*To be concluded.*)

May 3rd, 1909.

THREE CASES OF EXTRA-PERITONEAL RUPTURE OF THE BLADDER.

By E. W. ROUGHTON, B.S.Lond., F.R.C.S.,
Surgeon to the Royal Free Hospital.

CASE 1.—A man, æt. 21 years, was admitted to the Royal Free Hospital on July 8th, 1907, having been run over by a loaded van; one wheel had passed over his pelvis.

On examining the pelvis it was quite easy to approximate the spines of the ilium by making moderate pressure with the hands; there was obviously a fracture of the pelvis. He was unable to pass water. A catheter was easily passed into the bladder and drew off four ounces of blood and urine. It was not considered necessary or advisable to inject a measured quantity of fluid into the bladder.

Supra-pubic exploration was performed at once, the peritoneal cavity being opened; the peritoneal aspect of the bladder was free from injury. The reflection of peritoneum was then pushed up from the anterior surface of the bladder and a rent about an inch long discovered. The cellular tissue was infiltrated with bloody fluid and a fracture could be felt at the right ilio-pectineal eminence.

The peritoneal cavity was then closed and the rent in the bladder sewn up with a continuous catgut suture not piercing the mucous membrane. A drainage-tube was placed in the pre-vesical space and the skin wound drawn together with two or three interrupted sutures.

For the first two days a catheter was passed every four hours. On July 10th there was some leakage of urine through the supra-pubic wound; a soft rubber catheter was tied into the bladder. Any fluid collecting in the retro-pubic drainage-tube was continually aspirated by a syphonage arrangement to be described presently. The wound was soundly healed by August 17th, viz. seven and a half weeks from the accident.

CASE 2.—A man, æt. 44 years, was admitted to the Royal Free Hospital on January 17th, 1908. He had been squeezed between two motor buses in a garage. He had passed water about four hours before the accident but not since.

His pelvis was found to be fractured. A catheter readily entered the bladder and withdrew five or six ounces of blood and urine. No measured quantity of fluid was injected. Supra-pubic exploration performed at once. Cellular tissue behind recti infiltrated with blood. Peritoneal fold pushed up and a moderately full bladder exposed. Peritoneal cavity not opened. The bladder seemed to be intact. A comminuted fracture of the pelvis was readily detected near the left ilio-pectineal eminence; a loose splinter was removed. The bladder was then incised and several ounces of blood-stained fluid and clot evacuated. A caisson speculum was introduced and the bladder sponged dry; a rent about an inch long was then visible near the left side of the trigone; no attempt was made to sew it up as it was quite inaccessible. A large drainage-tube was introduced into the bladder and the incision drawn close around it by a couple of catgut stitches; the pre-vesical space was drained and the abdominal wall drawn together by a few interrupted sutures. The bladder was continually aspirated by the syphonage apparatus for three weeks; the pre-vesical drain was removed after eighteen days. Urine was passed *per urethram* on the twenty-fourth day; good recovery ensued.

CASE 3.—A youth, æt. 17 years, was admitted to the Royal Free Hospital on March 14th, 1908. He had been squeezed between railway buffers whilst shunting. The pelvis was fractured. A catheter was passed into the bladder but no urine was withdrawn; the eye of the catheter was found blocked with clot. Without further investigation the patient was anæsthetised and supra-pubic exploration performed. The fracture was found to be situated in the horizontal ramus of the pubes on the left side. The peritoneal fold was pushed up and the bladder found to be moderately full. No rupture was visible. The bladder was then opened and its contents, which consisted chiefly of clotted blood, sponged away. At first the interior of the bladder seemed to be undamaged, but on further search through a caisson speculum a small hole, scarcely more than a puncture, was found on the left front of the bladder, that is to say, in the part of the bladder-wall nearest the fracture. The

puncture was not sewn up. The bladder and pre-vesical space were drained in the same manner as in the second case. Recovery was delayed by the wound suppurating, but was eventually entirely satisfactory.

These three cases illustrate very well the symptoms, diagnosis and treatment of extra-peritoneal rupture of the bladder due to fractured pelvis. In all three cases the pelvic fracture was easily recognised by pressure on the iliac crests, and subsequently confirmed by digital examination through the supra-pubic wound. In all three cases the urethra escaped and a catheter was easily passed. Drawing off a mixture of blood and urine gave sufficient evidence of damage to the bladder. No attempt was made to test the presence of a rent by injecting a measured quantity of fluid; had one done so in the third case it is almost certain that an equal quantity of fluid would have been withdrawn, as the rupture was too small to allow anything to pass through it without using more pressure than would have been advisable, and thus doubt would have been thrown upon the diagnosis.

In Case 1 I opened the peritoneum and investigated the peritoneal aspect of the bladder first; in the other two cases I opened the bladder and examined it from within. I think the latter is the better procedure in cases of ruptured bladder due to fractured pelvis as the rent is much more likely to be extra-peritoneal. There is no difficulty in opening the bladder as it is sufficiently distended by blood and urine; the extravasation of blood into the cellular tissue renders the lower limit of the peritoneum easier to define and displace.

It is by no means essential to sew up the rent in the bladder-wall. In Case 2 it would have been extremely difficult if not impossible to sew it up, and in Case 3 there was really nothing to sew up. I do not think that Case 1 derived any obvious benefit from having the rent sutured.

The most important part of the treatment is drainage. Urine must not be allowed to run out of the bladder and infiltrate the pelvic cellular tissue. The pre-vesical space is drained by a tube in the usual way. The bladder is best drained in the following manner. A rubber tube as thick as one's thumb is placed in the bladder. It should be long enough to project about two inches above the skin, and should have a V-shaped notch cut in its intra-vesical end so as to facilitate urine entering it. From a two-gallon jar standing on the locker alongside the bed, water is slowly syphoned off into a receptacle on the floor by means of a long rubber tube. A No. 10 or 12 rubber catheter is joined to a two-foot length of rubber tubing (by means of a short glass tube) and made to anastomose with the syphon tube by means of a Y-shaped piece of glass tube. The end of the catheter is passed down to the bottom of the intra-vesical drainage-tube and kept in position by a safety-pin or a piece of strapping attached to the bandage covering the dressings. When the water flows along the syphon tube it creates a negative pressure in the catheter and so sucks out the urine from the bladder. The flow through the syphon must be slowed as much as possible, otherwise the jar will require to be replenished too frequently. This is best done by cutting the syphon tube and joining the divided ends with a piece of lead pipe, the sides of which are squeezed together until the water issuing from the end of the tube is a stream which almost immediately breaks up into separate drops. In this way the water runs away at about the rate of a gallon an hour, in other words the jar must be replenished at least every two hours.

It is hardly necessary to add that asepsis is of essential importance.

May 3rd, 1909.

Blaschko says that neither the fact that Wassermann reaction may be obtained in certain diseases, such as framboesia, sleeping sickness, and scarlet fever, as well as in syphilis, its clinical value is but little modified by this fact. Scarlet fever is easily distinguished from syphilis, while the other diseases are very rare in Europe. Blaschko reports his experience with one thousand patients in whom the reaction was tried. In over thirty cases the reaction was negative, though the diagnosis of syphilis could be made on other grounds; tabes dorsalis and syphilitic disease of the bones were most frequently represented among these negative results. Blaschko has also observed ninety cases in whom a strong positive reaction was changed by thorough antiluetic treatment into a weak reaction, or was made to disappear altogether.—*Med. Record*, vol. lxxv, No. 15

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A CLINICAL LECTURE

ON

HEMIANÆSTHESIA OF THE DISSOCIATED FORM.

Delivered at St. Bartholomew's Hospital.

By W. P. HERRINGHAM, M.D., F.R.C.P., Physician to the Hospital.

GENTLEMEN,—The case I shall talk to you about to-day is a very unusual case, one I have never seen an example of before. And although I do not usually talk to you about very out-of-the-way cases, this is so instructive that I think it is worth bringing before you. The patient is a man, æt. 36 years, who has been in good health up to the middle of last year. In July of last year he came to the out-patient department with the symptoms of which he is now complaining—that is to say, in July last he complained of staggering, and he says he used to sway chiefly to the left when he walked. It was also noted at the time that he came that he had facial paralysis on his left side. He also had nystagmus when looking sideways and when looking upwards. Also he had diplopia when looking to the left, which means probably a slight weakness of the left sixth nerve, so that he could not turn his eye out so much as he could turn his right eye in. Also, at that time his left pupil was smaller than his right. At the same time he had the great symptom which he now has, and which is the reason I bring his case before you, that is to say he had what we call "dissociated anæsthesia" occupying the whole of the right side of his body and the right side of his head and neck. He remained as an out-patient until December, and he was admitted into the hospital on December 10th. And his story was that for the last month he had had frontal headache, and for the last ten days at least he had been vomiting almost every day, the

vomit being of what we call the "cerebral type," that is to say, not produced immediately by taking food, but coming on at odd times, either of the day or night. When he came in to us we noticed that he had practically the same symptoms as he had been complaining of in the out-patient department. What he said about his vomiting was quite correct, that he was vomiting, just like a cerebral case, repeatedly, and that went on for some time after his admission, and the headache also continued severely for some time afterwards. The first thing I thought of in a case in which there was vomiting, headache, and some disorder of movement, was cerebral tumour. But repeated examinations of the discs showed no abnormality whatever, and that has been the case throughout the illness. And there has been no abnormality in the fundus of his eye. You will find that his disorder of movement is of a certain peculiar type. He staggers when he walks, as you will see. It is the staggering of a man who cannot maintain his equilibrium; it is not like locomotor ataxy, in which the legs run away with the man. And it is not a case of weakness of the legs in which the person cannot move the legs because the legs themselves are paralysed. If you watch him repeatedly, as we have done in the wards, there is no question that he has the gait of a man who cannot keep his equilibrium. That is typical of disease in the region of the cerebellum; it is not typical of any spinal disease. When he opens his jaw you will notice that it moves sideways, and that is significant of paralysis or weakness of one of the external pterygoids. There is some weakness of the motor division of the fifth nerve on the left side. He has, or had, marked nystagmus on looking to the left. He told us plainly that he had diplopia when he looked to the left, and that was probably due to weakness of the left sixth nerve. There is also some weakness of the left seventh or facial nerve. He does not wink so well with his left eye, and the left naso-labial fold is less marked than the right. The involvement of the eyelid shows that the facial is affected either at or below its nucleus in the base of the brain. But his resistance to force used against his arms is good. There is no trouble with his sphincters. He has very marked ankle-clonus on the right side, very slight on the left. On neither side can we obtain the extensor response which goes by the name of the Babinsky sign. And he has no inco-ordination of his arms or hands when he is lying down in bed; if you hold up the finger quickly he can touch it with either hand just as readily as can a normal person. And next comes the main feature of the case. The whole of the right side of his face and body has lost the sense of temperature and the sense of pain; he does not know the difference between hot and cold test-tubes, nor the difference between the head of a pin touching the skin and the point of a pin plunged fairly deeply in, anywhere on the right side. So he has this well-marked group of symptoms which we call dissociated anæsthesia occupying the whole of the right side of his body, and certain symptoms pointing to involvement of cranial nerves at the left side of the base of his brain. Dissociated anæsthesia is a symptom which has been noted for many years. It has been long known that certain lesions of the central part of the spinal cord produce a loss of the sense of temperature and a loss of the sense of pain, although the sense of ordinary touch and muscular sense are preserved. And it is almost entirely owing to the discoveries of morbid anatomy that physiologists have been able to trace the path of the sense of temperature and of the sense of pain up the spinal cord. Everybody now knows that whereas all the sensory fibres enter the posterior horns, the fibres of common touch and of the muscular sense pass up in the posterior columns, while, on the other hand, since a lesion of the central grey part of the cord interrupts the sense of pain and of temperature, it is obvious that these fibres run into the central grey matter. That was proved by cases of syringomyelia and various other forms of central disease. But it is also proved that these fibres of pain and temperature do not remain in the central grey matter, because a local lesion in the central grey matter such as a small tumour or cavity only interrupts these particular sensations over a certain area of the skin, and not over the whole surface of the body below the level of the lesion. It is therefore clear that these fibres, after remaining a little distance in the grey matter, pass out again and do not go right up in it. And the evidence of ascending degeneration on the one hand and of very few cases of localised lesions on the other show that they reach the antero-lateral tract and go up in this situation to the brain. For a long time that

was all that was known of them. But during the last twenty years a few cases have been collected, of which that which I have shown you is one. They are very uncommon cases, and I believe only twenty-five or thirty are known. They have shown this very uncommon combination of dissociated hemianæsthesia, sometimes of the whole of one half of the body and head, sometimes of one half of the body and the other half of the head, combined with certain cerebral symptoms, which indicate that the lesion is somewhere near the base of the brain. A few of these cases have come to the post-mortem room, and a very extraordinary and quite unexpected lesion has been found, a lesion connected with a certain small artery that no one would have supposed would have been of any consequence. As the vertebral artery goes up it enters the spinal canal, and the two join to form the basilar. Immediately before they join they give off two branches, an anterior spinal on each side, and a posterior inferior cerebellar artery. This latter winds backwards round the outer edge of the medulla oblongata, between the roots of the two nerves. On its way back it gives branches to the olivary body and the parts about it, and the lesion which has been found in these cases has been a thrombosis of that little artery with a corresponding patch of softening where I have drawn a dotted line. That area contains many of the fibres connected with the sense of equilibrium coming from the spinal cord. The softened patch here shown in the cases which have come to post-mortem examination apparently contains the fibres which convey the sense of temperature and pain. That post-mortem discovery has taught us what we never knew before—the position of the fibres of pain and the fibres of temperature at this level of the central nervous system. These fibres are between the corpus restiforme behind, and the olivary body in front. That situation explains the curious cranial combinations which you get in these cases. They are by no means always the same. In this case of mine the state of affairs is that which is represented in this diagram; the loss to the sense of heat and of pain goes right up to the top of the head on one side only. But in some cases it is crossed at the neck, so that whereas the left side of the trunk and limbs is anæsthetic, the right side of the face is affected. That is called "crossed dissociated hemianæsthesia." The difference depends probably upon the level of the lesion, and it shows us that the temperature fibres and the pain fibres belonging to the fifth nerve, which you know are supposed to be derived from the ascending or spinal root which I have marked in the diagram, cross over very quickly just as do the similar fibres of the posterior spinal roots, and it is according to whether the lesion is at a lower level or at a higher level where the fifth nerve has completely crossed that you get a dissociated hemianæsthesia which is crossed or uncrossed. This man, and many of the other patients whose cases have been recorded, has facial paralysis of the opposite side, and that is explained by the position of the facial nerve and nucleus which I have marked. It is close to the situation where this softening takes place. The facial fibres curve round the nucleus of the sixth nerve of the same side, uncrossed. All the sensation fibres have crossed over from the opposite side. But the cranial nerves are coming out from the same side, so the motor symptoms are on the opposite side to the sensory. The glosso-pharyngeal and vagus are sometimes involved, and they produce curious difficulties in swallowing, which has been a marked feature in some of the cases. That is not so in my case. The staggering is obviously connected with the passage into the cerebellum of these fibres from the spinal cord which go into the corpus restiforme. This latter part has nearly always been involved in the cases which have been recorded and which have been examined post-mortem, which have been only three or four in number. There is no doubt that the corpus restiforme takes to the cerebellum the fibres which run from the spinal cord conveying the sense of equilibrium. So it is a remarkable, unusual, and, topographically, an extremely interesting case.

The question of the pathology of the condition is, of course, unsettled. I cannot tell that he has thrombosis of the posterior inferior cerebellar artery; I can only say that there is a lesion somewhere about that region.* The extraordinary fact remains that the lesions which have been seen have been due to that particular disease—thrombosis in an artery which you would not expect to have any importance in the nervous system. The reason why it is of importance is this: that although the termination of the artery, when it goes round the cerebellum, anastomoses freely with the opposite side, also with the posterior superior cerebellar, yet its branches which it gives off on its way round are terminal arteries, and have nothing to anastomose with. So if it is blocked on its way round, these little arteries are blocked and there is no blood supply for the area which they serve.

I have some diagrams here by which some of the other recorded cases have been illustrated.

* The patient is since dead. Optic neuritis appeared at last, and a tumour was found in the situation expected. The case will be published in full.

May 10th, 1909.

WITH MR. LOCKHART MUMMERY IN THE OUT-PATIENT DEPARTMENT OF ST. MARK'S HOSPITAL FOR FISTULA AND DISEASES OF THE RECTUM.

THIS man, æt. 42 years, a warehouseman, originally came up with tubercular ulceration of the anus and rectum. When he came first he had extensive ulceration all round the anus, bad chest symptoms, with phthisis in the left lung, and a considerable discharge of blood from the bowel. We took him into the hospital for a time to examine him; it was decided than an operation would do him no good, so he was advised to go down to the country. He has been in the country nine months. In view of the serious condition of the lung and the fact that there was tubercular ulceration it was decided that operation on the anus would be useless, and so we advised him to get away. The improvement in his condition has been quite remarkable. He has now picked up wonderfully; he has no cough, and his chest symptoms have cleared up. His rectum also has healed. It is a very good illustration of the fact that it is a mistake to operate upon these tubercular conditions of bowel where there is general tuberculosis, unless you can combine it with sanatorium treatment or residence in the country. He was about 8½ st. in weight when he first came to us, but he is now 9 st. 12 lb., although of only medium height.

Here is an elderly man, who comes complaining of diarrhœa, the symptoms having begun about eight months ago. And in a man of his age there is always the possibility of there being malignant disease. In cases like this the sigmoidoscope is of very great value. I pass the sigmoidoscope on this man and you will see I can do it quite well without an anæsthetic, there being but little discomfort to the patient. Notice that we dilate the bowel by a puff of air in advance of the end of the sigmoidoscope tube, so that the tube really need not touch the sides of the bowel at all. I saw through the sigmoidoscope that he has some catarrh of the bowel, but nothing to indicate the presence of any malignant disease. I am now looking into the sigmoid flexure itself, and I can distinctly see the left common iliac artery beating through the wall of the bowel, showing we are just below the bifurcation of the aorta. We shall give him some mist. hæmatoxylin opiatus.

This man is æt. 29 years. He had pruritis ani for a year, there was bad itching, and it used to keep him awake at night and generally caused him considerable trouble. On looking at the bowel we notice a wash-leathery appearance all round the side. It is getting better as the result of treatment. We have treated him twice by painting over this area with 20 gr. to the ounce nitrate of silver solution. The first necessity in pruritus ani is to find out the cause. When you get a case of pruritus ani, first examine the outside of the anus at the margins, to see if there are any tags, a fistula, a fissure, or an abscess. Then examine the interior of the bowel to see if he is suffering from piles or polypi. Then examine the highest part with a speculum to see if there is proctitis. Chronic proctitis or catarrh high up in the bowel seems to be a common cause of this itching about the anus. A common condition also is worms. For worms you have to examine the stools. Piles cause leakage; there may be a polypus or a little fistula, or there may be a posterior ulcer on the wall of the bowel. And these things must be examined for. But after a careful examination in a certain number of cases you will find absolutely nothing. There is no apparent cause for the condition whatever. Those are difficult cases to treat. Of course where there is an obvious lesion, such as piles, you treat that condition by operation before you do anything for the pruritus itself. But it is not safe to promise the patient the operation will necessarily cure his pruritus. But any treatment which does not take into account the cause of the trouble is not likely to be successful with regard to pruritus. This case was treated by painting the area in which the irritation occurs with strong silver nitrate, 20 gr. to the ounce, and in many of these cases the improvement is very great, as I have already said. There are points to pay attention to in applying it. Of course, if you put vaseline on your finger and put it into the bowel and then paint silver nitrate on that it is useless because there is a layer of vaseline all over the skin, and the silver nitrate never actually touches the skin. In such cases you must use soap for examining the rectum and afterwards wash it off,

so that there is no grease or anything of the sort to interfere with the effect of the silver nitrate. In cases of pruritus ani very satisfactory results can be obtained by patience, and especially by attending to the hygiene of the anus. I tell patients to not only keep the parts clean but dry. I prescribe powders or, at all events, lotions instead of ointments, so that the parts do not get into a soppy condition. You must also tell the patients to avoid alcohol and tobacco smoking, to lead a simple life, and not to sit on very soft seats. Many of them get very much better though they are liable to have a relapse. There are certain cases in which, apparently, after any sort of treatment they get so bad that life is intolerable. Application after application is given, but very little benefit results. In those cases the best treatment is Ball's operation—that is to say, an operation in which you make two semi-circular flaps, the bases of which correspond to the anus. These are dissected up to above the white line or mucocutaneous junction, so as to divide all the small nerves which run to the skin over the area of irritation. It is on the same principle as the operation for "tic douloureux" or trigeminal neuralgia. When the flaps have been sufficiently dissected up they are stitched back into position. By this means you have anæsthetised the whole area in which irritation occurs.- That operation certainly cures the pruritus for the time being, and in the majority of cases the cure is permanent. Of course, the first effect of the operation is to produce anæsthesia of the anus and surrounding skin. But the sensation to the parts returns in from three weeks to a month. As a rule the irritation does not return although the sensation does. Sir Charles Ball says it is an absolute success in all cases. I could not agree to that, but I have seen remarkably good results from it. One lady had had sixteen operations for pruritus of one sort or another. She wanted to join her husband in Ceylon, and she dare not go to a hot climate because of the irritation. I performed Ball's operation for her, and when I saw her two years later she told me she had never had a day's irritation since. I have never seen the flaps slough from this operation, but, of course, it wants doing carefully, and in order to do it you must have had some experience of rectal surgery. Ball's operation is vastly preferable to the former operation of burning the skin and pure nitric acid applied to the anus. There is no doubt Ball's operation is a scientific procedure, and it cannot result in stricture or other injury if properly performed.

This next patient complains of slight bleeding and discharge when the bowels act. On separating the anus I pull down a small internal pile which prolapses through the sphincter and is irritated by the rub of his trousers, causing bleeding. It is a mistake to suppose you can feel piles—you cannot; you can only see them. You may be able to feel inflamed piles. We are prescribing for him unguentum hamamelis to be used locally, with confection of senna to keep the bowels acting easily.

Here is a man, æt. 66 years, who comes with pruritus. He says he has had irritation and pruritus ani for the last three years. It itches badly at night and keeps him awake. We can see where he has been scratching and rubbing it; there is a certain amount of leakage through the anus, and as a result we notice that the parts are damp. That has caused this appearance. The appearance which you see is not the cause of the pruritus, but the result of it. If we stop the pruritus the appearance will disappear. On separating the buttocks we see there is an internal pile, which comes down on the left side, and you will see it never really goes up, and directly he gets into the standing position the pile comes partly through the sphincters, and remains there. So that the anus does not close itself up properly. A little mucus from the bowel leaks out, and the skin of the anus is kept in a sodden œdematous condition, and that is why he gets the itching. It is a typical case of pruritus resulting from an internal pile which prolapses and prevents the anus closing satisfactorily. The treatment is to take him into hospital and remove that pile. He has another pile in front. The only two specula worth using, in my opinion, are this little one, which is conical and has very thick metal edges and therefore does not hurt the patient, and the other is Kelly's tube, which, if it is properly passed, does not hurt either. The speculum to be careful not to use is the so-called bi-valve speculum. The separation of the two halves of that instrument hurts the patient, and moreover, when you have it

in position if you pull it out open it hurts the patient, and if you close it before trying to pull it out it nips the mucous membrane of the bowel.

Here is a man, æt. 51 years, whom I operated upon two years ago for epithelioma of the anus of enormous extent. It had been existing twelve or thirteen months, and was found to involve the anus and the whole of the rectum, and was protruding. We thought it was a practically hopeless case. I took the entire rectum away—skin, anus, sphincters, everything—closed the end of the bowel, dropped it into the peritoneal cavity, and closed the peritoneal cavity and the skin wound. I then opened the abdomen, drew out the end, and formed a permanent colotomy. That was done two years ago last December, and you see how fit and strong he is. He is a stevedore at the docks, and works like any other man. He also worked in the Blackwall tunnel. He has fought a man three rounds at Wonderland since the operation. He keeps himself quite comfortable, and you will see on examining the perinæum that there is a perfectly sound scar and no opening of any description. Of course we took away the coccyx also. People say a great deal about the discomforts and inconveniences of colotomy, but those disadvantages are often exaggerated, and here you see a man who has for the last two years been earning his own living by one of the most arduous forms of employment, and who suffers practically no inconvenience from the fact that he has a colotomy opening. In talking of the unpleasantness of a colotomy opening, people often forget to distinguish between cases where the patient is slowly dying from cancer of the rectum and cases where, except for the colotomy, the patient is quite well.

The next case is a woman, æt. 31 years, who is sent up with a note from her doctor stating that for the last three years she has been suffering from chronic mucous colitis, and that the symptoms have not improved in spite of careful medical treatment.

She tells us that she passes large quantities of mucus and casts, and that this is accompanied by attacks of severe abdominal pain. She has a constant pain in the abdomen, and suffers habitually from constipation. You notice that her complexion has a brownish or earthy appearance, and she looks as if she had lost flesh.

On examining her abdomen we find that there is some tenderness over the colon, especially on the left side, but otherwise nothing abnormal. By percussion we ascertain that the stomach is in its normal position, from which we may deduce that there is no marked ptosis of the transverse colon.

We will now examine the bowel. There is nothing abnormal to be found in the rectum, and the uterus and tubes are normal.

I now pass the sigmoidoscope for the purpose of examining the pelvic colon. We notice that the mucous membrane of the rectum and lower part of the colon is normal in appearance and shows no inflammation. This is important, as it proves that the case is not one of true colitis, as if there is chronic inflammation of the colon this lower part is almost always involved. On passing the instrument a little further we find that there is a very sharp bend or kink in the centre of the sigmoid flexure, and that the bowel at this part is fixed instead of being movable. This is almost certainly the cause of her trouble. There are adhesions fixing and kinking the sigmoid flexure and causing a chronic obstruction. On inquiry also she tells us that after the birth of her last child, which occurred a little time before the onset of the symptoms, she had severe inflammation, and was laid up for two months. This was probably perimetritis. The diagnosis therefore is chronic obstruction from adhesions in the pelvis, and the proper treatment will be to take her into the hospital and perform an operation. It is obvious that the ordinary medical treatment for chronic colitis will be quite ineffectual in her case, and it shows the importance of directly examining the bowel in such cases.

May 10th, 1909.

LHERMITTE, after reviewing the few cases in American and British literature in which acute cerebral compression from intra-cranial hæmorrhage was cured by evacuation of the blood, states that the measure is liable to give favourable and encouraging results in the cases which are extremely serious from the start, the patient being in deep coma, with hemiplegia persisting unmodified.—*Journ. A. M. A.*, vol. lii, No. 17.

SOME CLINICAL ASPECTS OF PERNICIOUS ANÆMIA.*

By HERBERT FRENCH, M.D.Oxon., F.R.C.P.Lond.,

Assistant Physician to Guy's Hospital; Pathologist and Lecturer on Forensic Medicine at Guy's Hospital; Late Radcliffe Fellow of Oxford University.

(*Concluded from p.* 62.)

(4) The Nerve Symptoms in Pernicious Anæmia.

Dr. Gulland, of Edinburgh, has drawn attention to the fact that nervous symptoms may not only be prominent in cases already known to be pernicious anæmia, but may also ante-date the recognition of the blood disease by weeks or months or even years.

I have seen a case in which the patient attended at a special hospital for nerve diseases for symptoms which were regarded as those of locomotor ataxy for upwards of two years before the cord changes were recognised as being associated with pernicious anæmia.

It is not at all infrequent to find various degenerations in the cord post mortem, particularly in the white matter, and when these are considerable the living patient may have presented symptoms suggestive of spastic paraplegia, ataxic paraplegia, locomotor ataxia, or simple ataxia, according to which parts of the cord were most affected. Peripheral neuritis may also occur, but it is difficult to say to what extent this may be due to the arsenic that is employed in the treatment of the disease.

It is less common, perhaps, for the complete signs and symptoms of any of the named diseases of the spinal cord to present themselves than for irregular nerve symptoms to appear, many of which are subjective, and, therefore, apt to be regarded as purely functional.

I shall presently read the notes of a case in which severe pains in the back, diagnosed as lumbago for lack of a better name, had been a prominent symptom for years before the pernicious anæmia was recognised. In other cases the nerve signs and symptoms—exclusive of headaches, gastric pains, giddiness, or buzzing in the ears, which are doubtless due to anæmia directly—were as follows:

Case 1: "I could not be sure of my foothold owing to numbness in my feet, and when I tried to walk I stumbled about like a drunken man."

Case 2: Paresis of the legs with ankle clonus on both sides.

Case 3: Knee-jerks sometimes present, sometimes not obtainable even with reinforcement.

Case 4: Paræsthesia of the thighs, with sensations in them described as their feeling "too hot inside and too cold out," quite unlike the ordinary sensations of the rest of the body.

Case 5: Delusional insanity of a dangerous type. The patient talked restlessly but incoherently to himself about such things as "pice," "mines just over the hill"; mixed a number of native Urdu words with his English; confused identities, failed to recognise his wife or relatives, apparently retained no idea of time or place; neglected the calls of nature, and required much care and attention. It might perhaps be thought that such a case was one of ordinary insanity, but the appearance of the patient and the following blood-counts showed that the mental symptoms were associated with pernicious anæmia.

Date.	Leucocytes per c.mm.	Red cells per cent. of normal (Thoma Leitz).	Hæmoglobin per cent. of normal (Haldane).	Colour index.
Oct. 4	8,000	24	38	1·6
Nov. 21	8,000	71	78	1·1
Dec. 12	—	64	74	1·15

Case 6: Ideas of grandeur and symptoms precisely like those of general paralysis of the insane.

Case 7: Hallucinations of sight, taking the form of a persistent notion that there was a large vase of flowers on the perfectly bare table; attributable, perhaps, to the position of the retinal hæmorrhages.

Case 8: Persistently extensor plantar reflex on one side, flexor on the other, without ankle clonus.

Case 9: Curious sensations in the thighs, knees, legs and feet, compared by the patient, who was a Scandinavian, to a feeling "as though she were always walking in deep snow."

* Delivered before the Medical Society of London.

Cases 10, 11, 12, 13, 14, 15: Numbness in the fingers and toes, hands and feet.

Case 16: Tingling in fingers and toes.

Case 17: Loss of power in both legs with increased knee-jerks and ankle clonus upon both sides.

Cases 18, 19, 20: Violent and severe sensations in the chest, compared sometimes to "tearing pains," and sometimes to a sense of the thorax being "tightly gripped and squeezed."

Case 21: Severe pains in the back with paresis of legs.

Cases 22, 23, 24 and 14: Absence of both knee-jerks.

Case 25: Absence of one knee-jerk, the other being present.

Case 26: Pains more or less all over the body, especially in the muscles, but without definite paresis.

Case 27: Pains in the chest and abdomen with general itching of the skin.

Case 28: Persistent extensor plantar reflex on both sides and scattered areas of marked paræsthesia in the legs, with sluggish knee-jerks and no ankle clonus.

Case 29: Increased wrist-jerks, elbow-jerks and knee-jerks; ankle clonus and extensor plantar reflex on both sides and rigidity of the legs.

These are the various nerve signs and symptoms presented by twenty-nine cases out of fifty-eight. The remainder did not spontaneously complain of anything similar, and nothing particular about the nervous systems attracted the attention of the ward-clerks who wrote the reports. If twenty-nine out of fifty-eight cases present nerve symptoms, however, of degrees varying from subjective numbness of fingers and toes to definite spastic paraplegia, it is clear that there is at least a possibility of a case of pernicious anæmia now and then being treated solely for nerve trouble unless some stress is laid upon the well-known possibility of pernicious anæmia being associated with pathological changes in the spinal cord and peripheral nerves.

(5) The Variability in the Colour Index in Pernicious Anæmia.

The final clinical criterion of pernicious anæmia at present is the occurrence of oligocythæmia with a high colour index and without leucocytosis. It is very important to realise, however, that the fact that the colour index proves to be low, or at least not high, when the blood is examined once only, or even more than once, is no proof that the condition is not one of pernicious anæmia; for when a series of blood-counts are made at intervals in the same case it is comparatively common to find that there are periods when the colour index is less than 1 as well as other periods when it is greater than 1. Roughly speaking, the index tends to be highest when the patient is most ill and anæmic, and to become lower as the condition improves. This is no absolute rule, however, for a high colour index may persist even when much improvement has recurred, and on the other hand a low index is sometimes found when the patient is very ill.

It is astonishing how quickly the index may vary: even when the instrumental error is reduced to a minimum in the hands of skilled observers there may he a high colour index one week and a low one the next; such radical changes in the character of the blood have been attributed to derangements known as "blood storms."

C. W—, cook (widow). Died May 16th, 1902.

Date.	Red corpuscles per c.mm. (Thoma-Leitz).	Red corpuscles per cent. of normal.	Hæmoglobin per cent. of normal (Haldane).	Colour index.	Leucocytes per c.mm. (Thoma-Leitz).
1901					
April 10	650,000	13	26	2·000	7000
May 15	1,800,000	36	41	1·139	5000
,, 26	1,800,000	36	40	1·111	7000
Sept. 20	1,800,000	36	60	1·666	—
,, 30	1,600,000	32	42	1·312	—
Oct. 2	1,512,000	30	33	1·100	—
,, 7	4,250,000	85	36	0·423	—
,, 11	5,050,000	101	40	0·396	—
1902					
April 3	785,714	16	25	1·562	6400
,, 23	699,000	14	20	1·429	9750
May 14	876,000	15	10	0·666	4800

Note.—Films were typical of severe pernicious anæmia.

The differential leucocyte count in April, 1902, was as follows:

	Per cent.
Small lymphocytes . . .	25
Large ,, . .	3
Polymorphonuclear cells . .	70
Coarsely granular eosinophile cells	2

C. R—, 46, housewife. Died June 24th, 1903.

Date.	Red corpuscles per c.mm. Thoma-Leitz).	Red corpuscles per cent. of normal.	Hæmoglobin per cent. of normal (Haldane).	Colour index.	Leucocytes per c.mm. Thoma-Leitz).
1901					
June 11	1,466,666	27	39	1·444	11,428
July 5	2,600,000	52	42	0·808	—
,, 18	3,160,000	63	75	1·190	—
1902					
Nov. 29	440,000	9	17	1·888	3640
Dec. 2	752,000	15	21	1·400	3800
,, 8	1,284,000	26	32	1·230	3400
,, 10	1,294,000	26	32	1·230	2800
,, 21	2,334,000	47	—	—	4600
,, 27	3,296,000	66	58	0·879	4600
1903					
Jan. 6	3,864,000	77	60	0·779	7032
June 6	683,333	14	20	1·429	8520

N.B.—440,000 red cells per c.mm. is probably one of the lowest counts on record, particularly in a person who none the less rallied as above.

Some of the series of counts already given, and these two additional ones that I give here, exhibit the fact that a pernicious anæmia blood may have a low colour index at times, and I think the point is one of great importance; it unfortunately adds to the difficulty of diagnosis, but it teaches that pernicious anæmia is not by any means to be excluded by a single blood count. I may add, perhaps, that the two last series of counts were made with a Thoma-Leitz's hæmocytometer, and a Haldane's hæmoglobinometer; moreover, the diagnosis was in each case confirmed by autopsy.

(6) The Injustice of the Epithet "Pernicious" in some of the cases.

I should now like to pass on to discuss an entirely different matter, and that is, the injustice of the epithet "pernicious" in some of the cases.

Pernicious in its lay sense is a very strong term, and I feel sure that its use leads the medical student to gather an erroneous idea of the prognosis in pernicious anæmia. It is true that hardly any patients in whom typical pernicious anæmia has developed ever become completely well again. It it also true that the fatal ending of the disease sometimes comes within a month or a few months of what seems to be the beginning of the disease. On the other hand, the average duration of pernicious anæmia from the time of its recognition until the patient dies is in a fair number of cases to be measured in years rather than in weeks or months; besides which the illness is not one of continuous downward progress like that of carcinoma of the stomach for example, for nothing in medicine perhaps is so striking as the way in which, even if the rally be only temporary, a patient who may seem to be *in extremis* from pernicious anæmia, with his red corpuscles under 20 per cent. of normal, may recuperate, not only once, but sometimes several times. If one were condemned to suffer from a fatal malady, but were given the choice between malignant disease of the upper part of the alimentary canal, for example, on the one hand, or from pernicious anæmia on the other, it is clear that in either case one might be dead within the year; but that if one chose pernicious anæmia one would have a better chance than with gastric carcinoma of living for several years.

The intervals between the recognition of the pernicious anæmia by blood count and the time of death in the forty cases, in which, out of my total fifty-eight, the ultimate fate of the patient is known, were as follows:

1 year or less, 25 cases	Less than 1 month	5 cases.
	1 to 3 months	8 ,,
	3 to 6 ,,	5 ,,
	6 to 12 ,,	7 ,,
1 to 2 years, 7 ,,	12 to 18 ,,	3 ,,
	18 to 24 ,,	2 ,,
	1 to 2 years	2 ,,
2 to 10 ,, 8 ,,	2 to 3 ,,	3 ,,
	3 to 4 ,,	1 case.
	6 ,,	1 ,,
	8 ,,	2 cases.
	10 ,,	1 case.

It will be seen that twenty-five cases died within the year, but that fifteen survived for one year or more, eight out of forty cases living for something between two and ten years after the time when pernicious anæmia had been diagnosed beyond doubt. The word "pernicious" is, I think, rather too strong to be applied to a condition in which the prognosis is no worse than this. Lymphatic leukæmia is far more pernicious a complaint than is pernicious anæmia. I should like to see the older term "Addison's anæmia" used instead.

It will be said that I have picked out a particularly favourable case when I give the following notes about Charles R—. The allegation is true; but his story illustrates so well both the power some of these patients have of rallying, and also the length of time they may survive, and further the fact that their initial symptoms—lumbago in this

case—may not seem to have any relation to a blood disease, that I beg leave to read this short account of him :

Charles R—, æt. 45 years, a bricklayer, was first admitted under Dr. Pavy, in 1889, for mental irritability, weakness in the legs, and pain in the back and loins. His colour at that time was not apparently abnormal and the diagnosis made was *lumbago and paresis of the legs*. The pains in the back were very acute, and the patient had had three or four attacks of it each year for the previous fifteen years. There was no hæmaturia nor other indication that the pains might have been due to renal colic, and lumbago seemed to fit the case. In view, however, of the subsequent course it seems at least possible that the pains were similar to those which other pernicious anæmia cases often complain of in one part of the body or another; for, less than a year later, in January, 1890, the patient was re-admitted for loss of physical strength, failure of appetite, diarrhœa and night sweating, and the skin was now pale and waxy and had been obviously so for more than two months. There were no retinal hæmorrhages but occasional specks of blood were expectorated. There was no other bleeding. The urine was high coloured; it contained no albumen, blood, nor sugar. The blood-count indicated pernicious anæmia. The patient was treated with pilula colocynthi et hyoscyami and mistura ferri et ammonii citratis, and improved in general condition though the blood-count remained much the same.

By September, 1891, the patient was so weak, however, that he could not work, though he had worked between his discharge and then. He was re-admitted under the late Dr. Washbourn and was in hospital from September 4th, 1891, to November 30th, 1891. The attacks of pain in the loins still continued and they were very bad. There were neither enlarged glands nor spleen, nor vomiting, nor diarrhœa. Treatment was now by means of liquor arsenicalis, which was increased up to nine minims three times a day, with material relief to the anæmia. The patient went out in November, 1891, and notwithstanding his "lumbago" remained well enough to work on and off for over four years before repetition of his old weakness and pallor compelled him to seek hospital treatment again. He was in from February 7th, 1895, till March 9th, 1896. He presented the typical pale yellow colour. His tissues were flabby but not wasted. The urine sometimes exhited a marked urobilin band spectroscopically, sometimes none. The temperature was typically up to 100° F. every night, and not below 98° F. in the morning as a rule. The nervous reflexes were natural. Arsenical treatment was adopted and some relief ensued. The patient was discharged able to walk about but unable to do labourer's work. He slowly relapsed and was re-admitted on March 1st, 1897. He seemed to get progressively worse, and yet he lived for two years after his discharge on May 20th, 1897. Mrs. R— writes on August 15th, 1907: "Mr. R— died two years after leaving Guy's Hospital, suffering from prostration and great pains in his head; it was indeed sad to see such suffering and the brain very much affected."

During his last stay in hospital his temperature was again typically between 99° F. and 100° F. each night.

The spleen, formerly not felt, now came two inches below the ribs, and the liver came one inch below the costal margin in the right nipple line. Ophthalmoscopic examination revealed neither optic neuritis nor retinal hæmorrhages.

The blood-counts were as follows :

Date.	Red corpuscles per c.mm.	Red corpuscles per cent. of normal.	Hæmoglobin per cent. of normal.	Colour index.
1890				
February	2,400,000	48	53	1·104
March	2,400,000	48	55	1·148
1891				
Sept. 18	1,400,000	28	28	1·000
,, 25	1,100,000	22	25	1·136
Oct. 5	1,800,000	36	35	0·972
,, 19	2,100,000	42	35	0·833
,, 26	1,800,000	36	36	1·000
,, 29	1,800,000	36	40	1·111
,, 31	2,000,000	40	40	1·000
Nov. 2	2,900,000	58	50	0·862
,, 9	3,350,000	67	60	0·895
1896				
Feb. 7	1,250,000	25	30	1·200
,, 13	1,500,000	30	35	1·166
,, 18	1,500,000	30	35	1·166
,, 24	1,250,000	25	30	1·200
,, 27	1,200,000	24	30	1·250
Mar. 9	1,000,000	20	25	1·250
,, 19	800,000	16	25	1·562
April 8	700,000	14	20	1·429
,, 22	1,500,000	30	30	1·000
May 2	2,150,000	43	32	0·744
,, 9	2,750,000	55	38	0·691
1897				
Mar. 1	3,000,000	60	30	0·500
,, 22	1,900,000	38	25	0·659
April 5	1,050,000	21	15	0·714
,, 12	650,000	13	16	1·231
,, 27	700,000	14	26	1·857

There was no leucocytosis.

Poikilocytosis and megalocytosis were well marked, and at times nucleated red cells were seen.

(7) The Difficulty Frequently met with in Accurately Dating the Beginning of the Illness, with some Thoughts that this Difficulty Suggests.

I have just referred to the length of time that elapses in different cases between the recognition of the pernicious anæmia and the death of the patient. The recognition of the disease is chiefly by means of blood-counts; but I should like to lay great stress upon the fact that in the majority of cases the blood-count recognition by no means coincides even with an early stage of the disease, much less with its actual beginning. When one reads through the histories of these cases as recorded impartially by medical ward clerks, one is struck again and again by the fact that symptoms have been present for months, years, or even many years before the anæmia itself becomes pronounced. I quite grant that there are a few cases which seem to be acute; in most cases, however, the onset is quite insidious and in quite a number the earlier symptoms are attributed to some entirely different malady—typhoid fever, for example, or English cholera when diarrhœa was a prominent symptom; a chronic nerve disease, as in Dr. Gulland's cases; functional disorder of the stomach in another type of case, and so on. I hope to publish the notes of all these cases in the 'Guy's Hospital Reports'; it is clear that I cannot read them all here.

The fifty-eight consecutive cases themselves dated their illness back for at least the following lengths of time prior to its recognition:

For less than 1 month	. in	2 cases
Between 1 and 3 months	. in	12 ,,
,, 3 and 6 ,,	. in	6 ,,
,, 6 and 9 ,,	. in	3 ,,
About a year	. in	11 ,,
Between 1 and 2 years	. in	9 ,,
,, 2 and 3 ,,	. in	4 ,,
,, 3 and 6 ,,	. in	7 ,,
For over 5 years	. in	4 ,,

I should like to recall the case of Charles R—, quoted just now, to illustrate what I mean. I see no lack of continuity in the history of his case from the original attacks of what appeared to be "lumbago" sixteen years before pernicious anæmia was diagnosed, to the patient's death from the latter disease eight years after it was recognised by blood-counts—twenty-four years altogether.

I could give many other examples of similar difficulty in deciding when the pernicious anæmia really began, but I will content myself with one more only, viz. the following:

Amelia P—, æt. 50 years, a ship stewardess, married but childless, was admitted on January 11th, 1905, and was discharged on February 24th, 1905. Her husband writes on August 19th, 1907: "After leaving Guy's my wife went to a convalescent home, from which she left very weak and ill. She rallied slightly when at home, some days comparatively well, others ill and depressed. She had a very bad colour, coppery shade. She suddenly lost consciousness, and finally died on April 1st, 1905."

When admitted she gave a history of increasing debility with vomiting, diarrhœa, and "indigestion" extending over four years and dating from an attack of "enteric fever" contracted at Naples. There had been many alternate remissions and exacerbations in her symptoms, which sometimes kept her in bed for weeks at a time.

Her spleen could be felt 1 inch below the ribs. The heart was a little dilated. There was marked numbness in the fingers and toes. Pyorrhœa alveolaris was present and was attended to by the Dental House-Surgeons. There was the typical evening pyrexia up to 99° F. or 100° F. Arsenical treatment was adopted, and although diarrhœa was often a troublesome symptom, the patient's general condition improved for a time. The improvement was short-lived, however, as has been noted above.

The blood-counts in this case were:

Date.	Red corpuscles per c.mm. (Thoma-Leitz).	Red corpuscles per cent. of normal.	Hæmoglobin per cent. of normal (Haldane).	Colour index.	Leucocytes per c.mm. (Thoma-Leitz).
1905					
Jan. 11	1,856,000	37	55	1·486	4200
Feb. 7	1,940,000	39	50	1·282	—
,, 22	2,020,000	40	55	1·375	4000

On inquiring into the nature of the "typhoid fever" in this case, it transpired that the symptoms

were mainly diarrhœa and pyrexia and that the patient was kept in bed for it for only four days. It seems clear, I think, that some name had to be given to an obscure febrile illness and that typhoid fever seemed to fit it at first; but time showed, I think, a direct continuity between that illness and undoubted pernicious anæmia. It might be urged that pernicious anæmia was not really present at the time of the "enteric" attack, but that the latter predisposed to it and was in a way its cause. I think, however, that our clinical knowledge of the disease is more likely to be advanced if we allow that the lumbago in the case of Charles R— and the diarrhœa and pyrexia in that of Amelia P— and other symptoms in other cases were really the earliest symptoms of a disease of which the later stages are characterised by profound anæmia, a high colour index, and a Prussian blue reaction in the liver. If this be so, then pernicious anæmia is the name for but a late phase of a more general disease which is at present unnamed. I would suggest a comparison between it and phthisis in this respect. It is not so very many years since it was impossible to diagnose early phthisis, and consumption was regarded as essentially fatal because it was only recognised when it had already passed beyond the stage when it was curable. The end of a phthisical person may even now be very rapid by galloping consumption, comparable to the acute cases of pernicious anæmia; or the end may be gradual with periods of recovery and relapse extending over months or years—comparable to the course of ordinary pernicious anæmia as we now understand that term; on the other hand, if recognised at a stage at which our grandfathers would have denied the existence of phthisis altogether, consumption may be completely cured; healed phthisis is found in a large proportion of post-mortem examinations at a General Hospital in patients who may never have been suspected to have had phthisis at all. I feel sure that pernicious anæmia as we know it is but a late stage of that which may be much commoner than we think, recovering spontaneously perhaps in many cases as phthisis does in others, breaking out into an acute phase in others, running a subacute or chronic up-and-down course in yet others. We are now able to recognise phthisis early, by bacteriological and other means, in a way that our forefathers could scarcely have believed possible. I hope that similar early recognition of pernicious anæmia will also become possible as time goes on. It is recognised far earlier now than it used to be; and, perhaps, if it were thought of and diagnosed earlier still some at least of the patients might be cured.

In conclusion, the points that I have tried to bring out are: First, that slight evening pyrexia is seldom absent in pernicious anæmia cases that are decidedly ill. Secondly, that pigmentation within the mouth of precisely similar character to that seen in Addison's disease may occur in pernicious anæmia cases treated with arsenic. Thirdly, that the spleen is to be felt in about one third of the cases, and that it is really enlarged. Fourthly, that nerve symptoms are not at all uncommon in pernicious anæmia. Fifthly, that the colour index of the blood, though typically higher than when an advanced stage of the disease has been reached, is not always nor continually high, especially during a period of improvement in the patient's condition, when it may be actually low. And lastly, that pernicious anæmia as we now know it is very possibly only a late and almost incurable stage of a disease which it is to be hoped will some day be recognisable early enough to be cured.

Mr. Leonard S. Dudgeon, in discussing the pathology of pernicious anæmia, emphasised the point that the blood in all the cases of pernicious anæmia to which he would refer gave a typical blood picture—namely, a diminution of the red cells to about 1,000,000 per c.mm., a high colour index, various degenerative changes in the red cells, great diminution or absence of rouleaux formation, marked poikilocytosis, few blood platelets, deficient fibrin formation, leucopenia, a relative lymphocytosis, and the presence of nucleated red blood-corpuscles—megaloblasts and normoblasts. There was no clinical evidence of any disease apart from pernicious anæmia in any of these cases, and in those instances where an autopsy was performed no cause was found for the severe anæmia. He next referred to the colouration of the serum. In nine out of the eleven cases the serum presented a yellowish-green colouration, which was quite distinctive. There was no reaction for bile-pigment, and it failed to give any spectrum. In the remaining cases this colouration of the serum was obscured by the presence of bile-pigment. He stated that,

in his experience, apart from pernicious anæmia, this reaction did not occur, even in three cases where the blood-picture was identical with that disease. In a paper published in the 'Proceedings' of the Royal Society, by Mr. Shattock and himself, it was stated that fat had been demonstrated in the leucocytes in the circulating blood in a large number of diseases, but, contrary to expectations, this phenomenon had not occurred in pernicious anæmia. The polymorphonuclear cells in this disease contained innumerable granules, which were opaque and stained a deep-brown colour with Scharlach R., but if the film preparations of blood were previously washed in any of the fat solvents these granules were found to be absent. It has been suggested that these granules might be related to the breaking-up of red blood-corpuscles owing to a hæmolytic action. If this view was correct we should have to admit that hæmolysis is continuously going on in pernicious anæmia; this, however, has not been shown to occur. Mr. Dudgeon stated that for some time past he had been carrying on investigations with normal and immune blood as to the presence of hæmolysins, hæmo-agglutinins, and hæmo-opsonins in various diseases. Special attention had been given to pernicious anæmia from this standpoint owing to the hæmolytic hypothesis, which many hold for the origin of this disease. In two papers received by the Royal Society he had shown that auto-hæmolysis did not occur, even when the immune serum was complemented, as far as his observations went, in pernicious anæmia, and that the immune serum also failed to hæmolyse normal red cells. In one instance the immune serum had a marked hæmolytic property on the red blood-corpuscles from a case of acute pneumonia, but to a less extent than that possessed by normal serum. It was shown that the serum from cases of pernicious anæmia had the same power to hæmolyse the red blood-corpuscles of a guinea-pig as normal human serum. In one instance the immune serum obtained at the post-mortem examination from a case of pernicious anæmia caused a high degree of hæmolysis of the patient's red cells, but it was found that this action was dependent upon a streptococcus present in all the blood-tubes. This organism was found to be the *Streptococcus pyogenes*, and was capable of hæmolysing normal and immune red cells quite apart from the action of serum. Further observations have shown that the immune red cells can be hæmolysed, however, in the presence of normal human serum. It was further shown that the immune serum from this disease was less potent in agglutinating normal red cells than the serum from other diseases. Auto-agglutination was never met with. In those examples previously referred to, where normal serum had been found to hæmolyse the immune red cells, hæmolysing agglutinins were similarly demonstrated and the specificity of this reaction was proved. It had been suggested that anæmia is dependent upon the presence in the serum of a substance or substances which allow the red cells to be taken up by the phagocytes in the blood. From the observations conducted in the present research there was nothing to support this view when the immune serum and immune red cells were incubated in the presence of normal leucocytes. As regards pernicious anæmia, however, it was shown, as in the case of the hæmolysins and hæmo-agglutinins, that phagocytosis of the immune red cells by normal human leucocytes occurred in the presence of normal serum. These observations on pernicious anæmia, and similarly in certain other diseases, lend great support to the view that the red cell itself must be reckoned with in observations on immunity. In concluding his remarks, Mr. Dudgeon pointed out that, although it was impossible up to the present time to demonstrate many of these most important points concerning the blood immunity of pernicious anæmia, yet it is known that phagocytosis of red blood-corpuscles (mainly by endothelial cells) occurs in the tissues in this disease, as also hæmolysis; but how far these changes are directly related to the terminal stages in the disease and how far to its actual source remains to be seen. He did not consider that there was any evidence to show that auto-infection by streptococci and the resulting auto-intoxication was in any way related to the pathology of the disease.

Dr. DE HAVILLAND HALL said he was not in a position to express an opinion on the pathological aspect of the question, and he could only admire the skill with which the facts were presented. But the clinical side of the subject had interested him very much of late years. As Dr. French had said, these cases were now more commonly recognised than a few years ago. The first point upon which

he was in accord with the author was as to the universality of a certain amount of pyrexia in these cases. He believed that all the cases of the disease which had been under his care, both in hospital and private practice, had had moderate pyrexia, and in a patient who died from the disease in hospital a few days ago the temperature was up to 102° or 103° F. During the whole of her stay in hospital she had had an evening rise. And in this patient the question of Addison's disease arose. He had been much interested in the remarks in the paper concerning the pigmentation which occurred in cases of pernicious anæmia treated with arsenic. In his patient there was an aspect like that of Addison's disease, precisely what one would expect in a well-marked case, except that there was only a suspicion of pigmentation on the buccal mucous membrane. There was also the apparently causeless vomiting which one usually associated with Addison's disease. But at the post-mortem examination there was no sign of disease of the suprarenal bodies. It was a very typical case of pernicious anæmia, running a very rapid course, with characteristic retinal hæmorrhages. Just as students had long been taught that they must not be content with a single examination for tubercle bacilli, so he thought the author of the paper had done good service by showing that one must not be content with a single examination of the blood in cases which were suspected to be pernicious anæmia. In fact several examinations should be made before a negative verdict was pronounced. And as Dr. French had mentioned, even when the blood examinations were made by skilled observers, the results seemed to vary from week to week. All who saw such cases must have been struck by the wonderful power of recuperation which they exhibited. Although when they came into hospital patients seemed to be almost dying, yet under careful nursing and the administration of arsenic the majority of them recovered, at all events for a time. Some of them went on for months and even years. Other cases, however, seemed to run a very rapid course. The patient who died on Friday had only been in the hospital a fortnight or three weeks. Owing to her constant sickness it was impossible to give arsenic by the mouth, because it increased the sickness. He therefore suggested that soamin should be injected intramuscularly. That was done for a week or ten days, but without definite signs of improvement, and as she began to vomit again it was discontinued. Therefore he thought the soamin had scarcely had a fair trial, but it was a method of treatment well worthy of consideration. He had heard of it having been extremely useful in lymphadenoma. Where there was great irritability of the stomach it might well be borne in mind, as it was evidently a very useful arsenical preparation. He agreed with Dr. French that it was a pity the term "pernicious" had been given to the disease. Patients were already depressed by their condition and the name added to that depression. It would be well if some name could be agreed upon which had not those objections. There were cases which were ushered in by jaundice, as Dr. Parkes Weber had mentioned. Two years ago a woman was admitted into Westminster Hospital, æt. 38 years, she having previously been well. She was suddenly taken ill with stomach symptoms and sickness, and with fairly well-marked jaundice. When he first saw the patient he pointed out to his class that she was a good illustration of catarrhal jaundice in middle age. The only point which seemed to be unusual about it was that it had not cleared up in three or four weeks, and afterwards there was no colour in the fæces or urine; it was, therefore, a case of acholuric jaundice, and for a week or so there was considerable doubt about the diagnosis. Fortunately he had the blood examined, and that revealed the true nature of affairs. The case showed the typical features of pernicious anæmia. She was immediately put upon arsenic, and in a month or six weeks she improved rapidly, and left the hospital with an almost normal blood-count. He had not heard of her for a year, but had asked a sister at the hospital to try to ascertain if she was still alive and well. Some cases of pernicious anæmia were ushered in by symptoms which seemed to suggest simple catarrhal jaundice.

Dr. WALTER BROADBENT said that two years ago he had two cases of pernicious anæmia under his care at the same time, and as he made studies of them he thought the methods of treatment he adopted might be of interest to members of the Society. The first patient was a man, æt. 39 years, who had been in the army twenty-one years, and was discharged in July, 1906, for pernicious

anæmia. He admitted the man to hospital in Brighton in November. He then had the typical lemon-yellow appearance, and was suffering from vomiting and diarrhœa, and his temperature was 99° to 100° F. at night, sometimes higher. The gums around the teeth were ulcerated and foul. His liver was enlarged two fingers' breadths below the costal margin, and the spleen about one finger's breadth. There was a history of past malaria and syphilis. He had thought the condition of the spleen was due to malaria, but possibly it was due to pernicious anæmia. The blood contained only 1,040,000 red cells. The colour index was 1·2. Megalocytes and poikilocytes were found, and among the leucocytes were some myelocytes. Arsenic was given in increasing doses, but in six weeks the red cells fell to 660,000. Dr. Broadbent then had X rays applied for ten minutes a day to the spine and the lower ends of the femur. That seemed to improve the condition of the blood, the count rising to 1,220,000, and the man was able to get up and walk about. But after a sudden rise of temperature to 103° F. for three days the red-cell count fell to 752,000, and the man became rapidly worse and had to be kept going by hypodermic injections of strychnine. He then asked the pathologist to the hospital, Dr. Bushnell, to see the case with him, and it was arranged that Dr. Bushnell should try to prepare a vaccine from any organism which he found to be predominant in the inflamed tooth-sockets. He isolated a streptococcus and found that the opsonic index of the patient's blood was 1·9 to that. But later it went down to 0·6. Then Dr. Broadbent injected two hundred millions of those streptococci as a vaccine. As the man seemed better for that, another injection was given two weeks later, and every fortnight for two months. The blood-count rose to 3,200,000 and the hæmoglobin to 78 per cent., while the patient was able to be up all day, feeling very well. An interesting point was that the tooth-sockets became absolutely clean, so much so that when the stock of vaccine was exhausted Dr. Bushnell was unable to isolate the same streptococcus again. After three months there was a relapse, and though vaccines made of another streptococcus were tried, and anti-streptococcic serum, the patient rapidly went downhill and died. The organism originally isolated corresponded to the *Streptococcus pyogenes* in that it did not clot or sour milk, though in some points it differed from the ordinary *Streptococcus pyogenes*. Shortly after that he had another case in, and he asked Dr. Bushnell to find some streptococci for that. The case was a typical one of pernicious anæmia. Dr. Bushnell obtained a staphylococcus and a pneumococcus from the gums. As the opsonic index varied to the staphylococcus they tried a vaccine of that for ten weeks, but it had no effect on the blood, though it cleared up the gum condition. Then he tried pneumococcus vaccine, but that again had no effect, no streptococcus was obtained, and she died. He thought the first case favoured Dr. William Hunter's idea that it was due to a streptococcus, and if one could happen on the right one, one might be able to prepare a vaccine which would do good to the pernicious anæmia in general. According to Dr. Dudgeon, normal serum seemed to be very bad for pernicious anæmia, because it would destroy any red cells which were left. In one case he had there seemed to be marked improvement when he injected fresh ox blood into the rectum. Probably it contained normal serum. He desired to ask what was Dr. Dudgeon's opinion on that. Dr. French, when speaking of pigmentation of the gums and its relation to the taking of arsenic, said that one of the patients developed pleurisy. He, Dr. Broadbent, had seen two cases of pernicious anæmia which were treated with arsenic in large doses develop pleurisy, and one case of Hodgkin's disease which was taking arsenic developed double pleurisy. He thought those pleuritic conditions were possibly due to the arsenic.

Dr. F. PARKES WEBER asked whether Dr. Dudgeon had had the opportunity of trying that very interesting test which he had mentioned, namely the hæmolytic action produced by adding normal blood-serum to the patient's red blood-cells during different stages of pernicious anæmia. If so, did the tests cease to give positive results during the periods of decided improvement? Dr. Dudgeon had also alluded to a peculiar colour of the blood-serum in cases of pernicious anæmia, a colouration which, he understood, was regarded by Dr. Dudgeon as characteristic of pernicious anæmia. This colouration might become a valuable aid to the diagnosis of pernicious anæmia if it were constant, and if it could be easily recognised clini-

cally, as he believed to be the case. It would be even more helpful if some definite chemical test could be found for the pigment in question. Whatever that pigment might be, he took it that the same pigment was probably present in the patient's urine, though the colour was of course obscured by that of other pigments in the urine; a chemical test might, however, be found to reveal its presence. Dr. French had spoken about very rapid improvement shown on consecutive examinations of blood. He asked whether Dr. French had in pernicious anæmia observed anything approaching the nature of what had been written about as "blood crises"—a sudden improvement in the quality of the blood accompanied by the appearance of a large number of nucleated red cells, some of them showing karyokinetic figures. It had been said by Dr. Broadbent that the giving of normal blood-serum by the mouth or subcutaneously was, according to Dr. Dudgeon's observations, likely to be harmful because it would favour hæmolysis. But he (Dr. Weber) did not think that was a necessary deduction. Even if it did have a hæmolytic effect it might possibly depend on the dose as to whether it did harm or not. Very minute doses might do good by provoking a "reaction," whereas large doses would probably have an unfavourable effect because the "action" of the dose would exceed the "reaction" on the part of the patient's organism. Probably the injection of vaccines might act in either way according to the dose employed. Large doses might do harm by their "action," whereas minute doses might do good by provoking a helpful "reaction." Similarly, mental factors (distressing or otherwise to the patient) might act favourably or unfavourably in cases of chronic diseases (including some chronic organic diseases as well as functional diseases) according to their strength and the kind of reaction which they provoked on the part of the patient's organism.

Dr. VINCENT BELL said it would be interesting to hear whether there had been noticed any particular geographical distribution of cases of pernicious anæmia. Did a disproportionally large number of cases come from the Fen districts? Possibly there might be some reason for the disease in the bacteria floating about in the air in those localities

Dr. FRENCH, in reply, said he thought apparently causeless vomiting was as common in pernicious anæmia as in Addison's disease. It was Dr. Hale White who first laid stress on the stomach symptoms in pernicious anæmia. Perhaps the vomiting both in Addison's disease and in pernicious anæmia really belonged to the category of anæmic vomiting emphasised by Dr. Beddard. With regard to the acholuric jaundice cases, he asked whether there was a decided yellowness of the conjunctiva in those referred to, because in all the cases records of which he had looked up at Guy's there had been no jaundice at all. [Dr. Dudgeon said the two cases of pernicious anæmia he took were not diagnosed as jaundice. Sir Almroth Wright mentioned some two years ago that bile-pigment was present in the serum but was not recognised clinically. Dr. Hall said he only spoke of one case in which he definitely noticed jaundice.] Dr. French, continuing, said jaundice was distinctly uncommon, but the slight pigmentation of the serum by bile in these cases might conceivably increase so as to become clinically evident. With regard to the foulness of the teeth, he had seen several pernicious anæmia cases in which the teeth were absolutely sound and good, and in which there was no jaw disease either, although he admitted that most cases of pernicious anæmia had very bad teeth indeed. It had been suggested by Dr. Broadbent that the giving of arsenic might have determined the onset of pleurisy where that occurred. In Hodgkin's disease he thought inflammation of various serous membranes was fairly common whether arsenic was given or not, but in pernicious anæmia inflammation of those membranes seemed to be distinctly rare even when arsenic was used. With regard to Dr. Parkes Weber's question concerning blood crises, he had called them in his paper "blood storms." He knew nothing about the geographical distribution of pernicious anæmia. The disease was often seen in subjects who had never been abroad, and also in people who came to Guy's from various parts of the world, but no particular regional incidence had been noticed. He had been surprised at the lack of mention of urobilin and tyrosin in the discussion. He would have liked to hear what relation urobilinuria bore to hæmolysis, and whether it could be used as a diagnostic in pernicious anæmia when the blood-count was by itself indefinite. Tyrosin was present as a spontaneous deposit in the urine in a small number of cases of pernicious anæmia. By extracting tyrosin from the urine and looking to see if there were crystals one might have an additional means of diagnosing cases. He believed the disease would seldom be recognised in its really early stage by examination of the blood alone.

Dr. DUDGEON also replied and the discussion ended.

May 10th, 1909.

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WITH MR. BLAND-SUTTON AT MIDDLESEX HOSPITAL.

VII.

CANCER OF THE GALL-BLADDER, BILE-DUCTS, AND DUODENUM.

GENTLEMEN,—Some of you may think I am wasting your time by devoting a whole lecture to the consideration of cancer of the gall-bladder, especially as the current text-books of surgery dismiss the matter in a short paragraph. It may also surprise you to learn that many works on general surgery written ten years ago contain no reference to this subject. Twenty years ago very little information concerning cancer of the gall-bladder was obtainable, and it remained more or less a pathological curiosity until the aggressiveness, enterprise, and resourcefulness of modern surgeons have shown that it is a frequent disease, and is of clinical importance. Moreover, the frequency with which cancer of the gall-bladder and gall-stones co-exist has invested the association with a great pathological and practical interest in connection with the cancer problem. In this lecture I intend to discuss the subject from the clinical standpoint, especially in its bearing on the influence of environment in enhancing the deadly consequences of cancer. I shall also consider the epithelial changes in their bearing on the cause of cancer generally.

At the outset it will be necessary to briefly review the epithelial arrangements connected with the drainage system of the liver.

Physiology teaches us that bile, like urine, is purely excrementitious, and the liver, in addition to its glycogenic functions, may be regarded as a great organic filter, which separates not only toxins from the blood conveyed to it by the portal vein, but also micro-organisms which enter the portal circulation from the gastro-intestinal tract. The method

by which the excrementitious bile is conveyed from the recesses of the liver to its outfall in the duodenum involves a brief consideration of the canal system of this organ. The bile-passages arise in the most intimate association with the hepatic cells; there is reason to believe that they begin as minute canals in the protoplasm of these cells, but it is certain that they become obvious to the microscope as minute intercellular passages, or bile canaliculi, which communicate with the bile-ducts ramifying in the interlobular connective tissue. The bile-ducts around the lobules possess connective-tissue walls and are lined with short columnar epithelium, but in the portal canals the ducts are larger and the epithelium is columnar. The bile-ducts converge to the portal fissure, and, enlarging as they

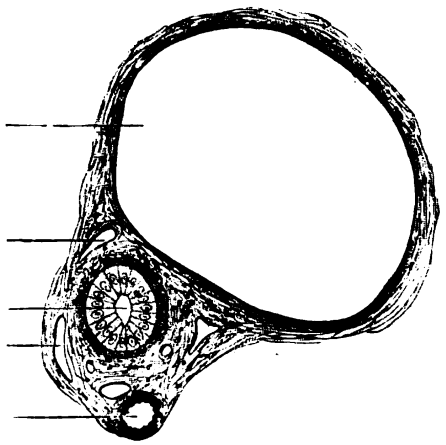

FIG. 1.—Transverse section of a portal canal, showing particularly the bile-duct with its epithelium. (After Schäfer.)

become confluent, issue as the right and left hepatic duct respectively. These conjoin to form the hepatic duct, which as it issues from the transverse fissure of the liver receives the cystic duct descending from the gall-bladder; together they form the common bile-duct, which opens into the second part of the duodenum.

From this account it will be seen that there is a continuity of epithelium from the duodenum to the inmost recesses of the liver, but it is customary and convenient to speak of the canals and canaliculi within the liver as intra-hepatic, whilst the larger ducts, from the points where the hepatic ducts emerge into the portal fissure to the termination of the common bile-duct in the duodenum, are usually termed the "excretory apparatus of the liver"; this consists of the hepatic duct, the cystic duct, the gall-bladder, the common bile-duct, and the ampulla (the diverticulum of Vater).

The epithelial perversion commonly known as cancer may arise in any part of this drainage system of the liver, but it is more frequent in the excretory apparatus than in the intra-hepatic canals.

Cancer arising in the portal canals or in the bile canaliculi is probably uncommon, and when present it is rarely amenable to surgery, indeed, it cannot be distinguished from carcinoma arising from the true hepatic cells until after death. It is of interest to the pathological histologist because, as Rindfleisch pointed out, a primary cancer arising in the intra-hepatic canals exhibits a tubular arrangement, and I well remember examining many years ago some sections prepared from cancerous nodules in the lungs, secondary to a primary carcinoma of the liver, which showed a series of tubules in section lined with columnar epithelium and possessing all the histological features of a bile-canal surrounded by normal pulmonary tissue.

It is not my intention to deal with intra-hepatic cancer, but to confine our attention to this disease as it occurs in the excretory apparatus, and as it is more common in the gall-bladder than in the main duct let us consider its leading features as we can study them in this receptacle.

Cancer of the gall-bladder.—This disease has attracted great attention in recent years; this is in a measure due to its frequent association with gall-stones and also on account of its excessive malignancy. Cancer arises in any part of the gall-bladder; the course of the disease and the clinical signs which accompany it are modified by the situation of the primary growth. The presence of gall-stones in cancerous gall-bladders is probably as frequent as 95 per cent.; let me in this part of my lecture merely mention the fact that many surgeons regard the existence of gall-stones in the gall-bladder as a pre-cancerous condition. I will offer you some criticisms on this matter in the next lecture.

In whatever part of the gall-bladder this disease arises it will tend to infiltrate the walls and fill its cavity with cancerous tissue; consequently when the disease has run its course it will be difficult. and, indeed, often impossible to decide the particular spot in which it started. This is well shown in the specimen on the table, which was obtained

after death from an old man: the gall-bladder is replaced by a mass of cancer containing a number of polygonal-shaped gall-stones nested in its centre, and were it not for this nest of concretions we should have been unable to detect the gall-bladder, so thoroughly have its tissues been destroyed. In a woman, aged 56, with a gall-bladder as big as a cocoanut, the cancer was represented by a pultaceous mass which gave rise to a sense of fluctuation on palpation; so distinct was this that it gave me the impression that the trouble was due to a calculous cholecystitis and that the gall-bladder contained fluid. This induced me to expose and open the gall-bladder. I found eighty-six almost pure cholesterin calculi resembling polygonal lumps of spermaceti embedded in the soft growth.

In another class of case the gall-bladder will not be much enlarged; its walls, however, will be thickened, very hard, and so tightly contracted on the gall-stones within it that they will be as firmly packed as a tesselated pavement, and efforts to extract them will almost invariably cause the concretions to break up rather than separate from each other.

Occasionally the cancerous process will start in a calculous gall-bladder, and without altering the contour of this receptacle will quickly infiltrate or permeate the adjacent tissue of the liver, and in a few months the dividing line between the gall-bladder and the hepatic tissue will be completely obliterated.

The number of concretions in a cancerous gall-bladder varies enormously. The museum of Charing Cross Hospital contains a gall-bladder showing a primary cancer arising at its neck and extending into the cystic duct. A solitary gall-stone is embedded in the cancerous mass.

The only example of a cancerous gall-bladder unassociated with gall-stones which has come under my observation happened to be the first I saw in a living subject. In this instance the disease arose at the fundus of the gall-bladder of a man and formed a patch of new growth, in superficial extent as large as a thumb-nail, but it infiltrated and penetrated the wall; a small bud-like process of growth, not larger than a currant, projected on the serous surface of the gall-bladder and infected the peritoneum. Every structure in the belly was beset with minute cancerous nodules. The abdomen was inconveniently distended with fluid. The physician in charge of the patient could not account for the hydroperitoneum, and at his request an operation was undertaken. The evacuation of many pints of fluid afforded temporary relief and established the diagnosis.

One of the most remarkable examples of this disease which has come under my notice occurred in an aged spinster, who knew for several years

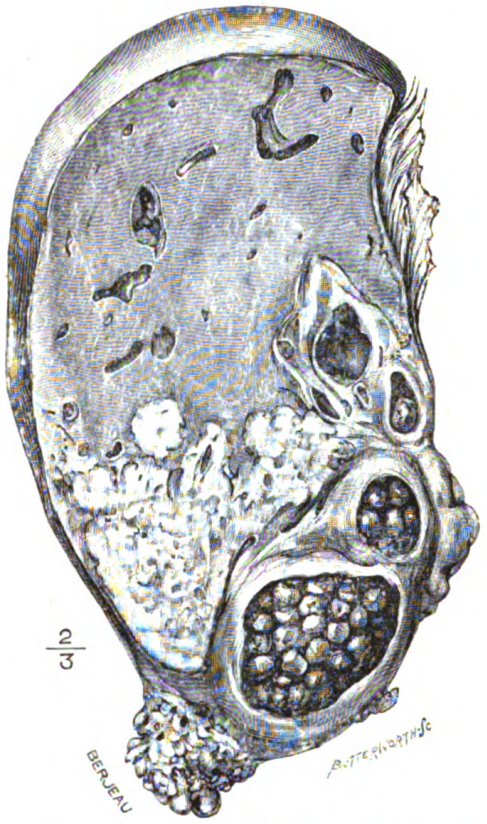

FIG. 2.—A cancerous and calculous gall-bladder in section, showing the manner in which the liver is infiltrated. (Museum of St. Bartholomew's Hospital.)

that she had a large abdominal tumour which was regarded as a subserous uterine fibroid with a long and slender pedicle. In course of time her health deteriorated, and free fluid (hydroperitoneum) collected in the belly. It was decided to evacuate the fluid and remove the tumour if possible. At the operation this tumour, which reached to the hypogastrium, proved to be a huge gall-bladder. I succeeded in removing it, and was disappointed to find numerous secondary nodules in the right lobe of the liver. After a thorough examination of the internal organs I failed to discover a primary cancer. After completing the operation an examination of the gall-bladder disclosed an extraordinary

condition. A calculus firmly impacted in the cystic duct had led to the production of the condition known as *hydrops vesicæ felleæ*, the largest example that has ever come under my notice. The large cavity contained two remarkable gall-stones, for one of them resembled an acorn and the other its cup (Fig. 3). The concavity of this shallow cup was occupied by the rounded pole of the balanoid calculus, and the two bodies had freely moved on each other, for their opposed surfaces are polished as the result of the trituration. The relation of these two gall-stones vividly recalled to my mind the glacier-mills, which form such interesting objects in the famous glacier garden of Lucerne.

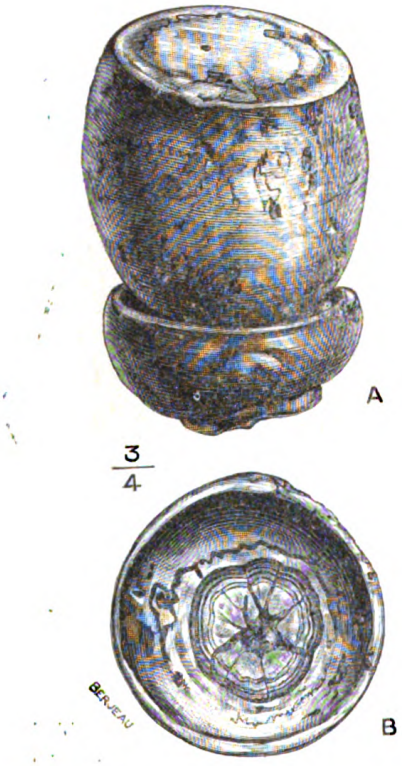

FIG. 3.—A. Two gall-stones adjusted in the form of a mill. B. The nether gall-stone with its polished surface exposed. (From a cancerous gall-bladder.)

So far as the patient was concerned the most sinister object in this huge gall-bladder was a patch of cancerous material infiltrating its walls and which was the source of the material causing the secondary nodules so conspicuous in the liver.

Gall-stones are often numerous when associated with cancer. The gall-bladder represented in Fig. 4 is remarkable in this respect, for it contained several hundred almost pure cholesterin calculi. The specimen is remarkable; I removed it from a woman, æt. 43 years, in whom it caused no pain; the patient was merely inconvenienced by the presence of a lump which she could feel in the abdomen. On examination it had the characteristic contour of an enlarged gall-bladder, but the unusual hardness of the mass made me regard it as cancerous.

FIG. 4.—An enlarged (cancerous) gall-bladder removed from a woman, æt. 43 years. The cancer had burst through the fundus of the gall-bladder and implicated the transverse colon. Eight inches of the latter was resected. Several hundred calculi, consisting almost entirely of cholesterin, were present.

When the organ was exposed in the course of the operation it had contracted an extensive adhesion to the adjacent omentum and transverse colon, for the growth, which filled the gall-bladder, had burst through the wall near the fundus, and, fungating freely, had infiltrated the wall of the colon. The neck of the gall-bladder was fairly free from the

cancer and the liver had escaped infiltration, but the implication of the transverse colon proved a serious matter, and in order to remove the disease I found it necessary not only to extirpate the gall-bladder but to resect eight inches of the colon and a large area of omentum. The cut ends of the gut were easily joined by suture, and the patient made a rapid recovery from the operation to die fourteen weeks later from recurrence.

The tumour on microscopic examination proved to be a perithelioma (endothelioma). This is a matter of pathological interest, because in most of the gall-bladder cancers which have come under my notice the subcolumnar and spheroidal type of cells prevailed.

In regard to the type of cells prevailing in cancerous gall-bladders, it may be mentioned that in an example which I removed from an elderly spinster the infiltrated walls of the gall-bladder were tightly contracted on the concretions. When the cancerous mass was examined in the laboratory it was found to be composed of typical squamous cells and abounded in cell-nests. This is an example of mutation of epithelium due to pressure, such as occurs in the intestinal mucous membrane exposed in a colotomy opening, or in the uterine mucous membrane covering a polypus extruded from the uterus into the vagina, and under other conditions.

The implication of the colon, which was such a prominent feature in this case, is a matter of importance in regard to diagnosis. Throughout this course of lectures it has been my endeavour to impress upon you the insidious way in which cancer arises in the viscera and makes steady progress without producing symptoms, until it so interferes with the function of the affected, or of the adjacent organs, that the life of the individual is in grave peril. This is illustrated in a striking way by the clinical signs present in a woman with a cancerous gall-bladder recently in my ward. She was sent in with a diagnosis of calculous cholecystitis. On admission I regarded an obvious tumour in the right hypochondrium as a cancerous lump in the tranverse colon, as it lay well below the line of the costal cartilages. At the operation it proved to be a cancerous and calculous gall-bladder; the disease involved the fundus of the gall-bladder and was firmly adherent to the adjacent colon. Though the patient was a spinster, aged 73, I succeeded without difficulty in extirpating the gall-bladder, and the cancerous nature of the growth was substantiated in the laboratory.

Cancer of the gall-bladder is more common in women than in men, and it is a disease of advanced life; probably the period of greatest liability is the interval between the fiftieth and sixtieth years. Cancer of the gall-bladder is most insidious in its beginning, notwithstanding the presence of gall-stones. The patients usually seek advice either on account of a local lump which they have detected or for a marked depreciation of health. In my experience there are two distinct conditions which present themselves in this disease. In one a more or less movable pyriform swelling exists in the right hypochondrium associated with a slight tinge of jaundice; this swelling resembles in all particulars an enlarged gall-bladder, but the local signs are not so acute as in cholecystitis, yet there is usually such an obvious impairment of the general health as to make one suspect the malignancy of the lump. In the late stages of the disease hydroperitoneum is present.

In the other class the patients come under observation with signs and symptoms indicating serious disease which resemble those peculiar to the gall-bladder, mingled with others pointing to cancer of the liver. In many instances it is impossible to decide from physical signs which organ is diseased until the parts are exposed in the course of an operation. In some instances the disease is proved to be calculous cholecystitis; in others it is a cancerous gall-bladder; in a few primary cancer of the liver, and occasionally a gall-bladder will be found to contain calculi, whilst the liver presents nodules of cancer, secondary to a primary focus of disease in some part of the gastro-intestinal canal. Occasionally the cancerous lump supposed to be the gall-bladder is situated in the transverse colon or the pyloric region of the stomach.

Primary cancer of the gall-bladder runs a rapid course, and usually terminates the life of the patient within six months of the onset of definite symptoms. Jaundice is present in the late stages of the disease in about one third of the cases.

Cancerous gall-bladders are sometimes successfully removed by surgeons, but when a large number of hospital cases are analysed the results cannot be considered encouraging. In the year 1905 seventeen patients with primary cancer of the

gall-bladder were submitted to operation in the chief general hospitals in London; of these nine died.

Unfortunately by the time a cancerous gall-bladder is discovered the opportunity for a successful operation has usually passed.

I shall discuss the relationship of gall-stones to cancer of the gall-bladder in the next lecture.

May 17th, 1909.

Vein Anæsthesia.—Bier has used this new method in 134 operations, including 10 amputations, 37 resections of joints, 12 sutures of bones, 7 extirpations of varices, etc. The results were perfect in 115 cases and satisfactory in 14, only 5 of the total 134 patients experiencing pain. The general circulation is cut off from the region to be operated on, and then the tissues are anæsthetised in this region by diffusion of the anæsthetic which is injected into a vein. The anæsthetic may be removed afterwards by flushing the vessels in the region with salt solution, if this is deemed necessary. No other method of local anæsthesia gives such perfect results, he declares. The constriction is applied with two elastic bands, the same band used for constriction hyperæmia, six feet long for the arm and ten feet for the thigh, wound around to cover a broad area above and below the field to be operated on, after the blood has first been expelled from the limb by winding from below upward. It is necessary to refrain from causing the least pain at the outset, as this destroys the confidence of the patient. He would refrain from the vein anæsthesia in case of senile or diabetic gangrene, but otherwise thinks this technique has no more contra-indications than any form of local anæsthesia. He has never witnessed any untoward by-effects of any consequence, and concludes his communication with the assertion that this form of anæsthesia represents a great advance; it throws all other methods of local anæsthesia into the shade, he believes, although he advocates it only when the ordinary measures for local anæsthesia are inadequate. ' Its special field is for major operations on the limbs. It supplants spinal anæsthesia for all such operations, as it is simpler and harmless.—*Journ. A. M. A.*, vol. lii, No. 18.

A CLINICAL LECTURE

ON

GOUT AND ITS TREATMENT.

By WILLIAM MURRELL, M.D., F.R.C.P.,
Physician to the Westminster Hospital, and Lecturer on Medicine and Clinical Medicine.

To attempt anything like a review of the subject of gout within the limits of a short lecture is to court failure, for the literature is so extensive that no man can master it. Acute gout, chronic gout, tophaceous gout, irregular gout, suppressed gout, saturnine gout, and many other varieties claim our attention, whilst the mere discussion of its ætiology and causation would occupy many pages. The most that can be attempted is to call attention to a few practical points, chiefly in the direction of treatment.

It is said with a certain amount of truth that joints which are rheumatic in youth are gouty in old age, the explanation being that a joint damaged by an attack of rheumatism, or for the matter of that by injury of any kind, is more likely to be attacked by gouty deposits than one which is sound. It would hardly seem likely that any confusion could exist between rheumatism and gout, and yet we are told on the authority of Dr. Futcher, of Baltimore, that in the Johns Hopkins' Hospital many cases of gout are mistaken for rheumatism even when well-marked tophi are present about the joints and on the helix of the ear. This may afford an explanation of the prevalent impression that gout is a rare disease in the United States. That it is less common in Scotland than in England is shown by the interest always taken by Scotch graduates, even those of wide experience, in the ordinary cases of the disease seen in our London hospitals. On more than one occasion I have noticed that visitors from the North have for the moment been distinctly puzzled by cases of this description which would prove no strain on the diagnostic powers of the average clinical clerk.

The age of the patient at the onset of the first attack is said to be from thirty-five to fifty, and it is usually regarded as a disease of middle life and advancing years. To this rule, however, there are many exceptions, and I have seen a well-marked attack in a boy at Harrow, and I remember a

house-physician of no great age who was periodically incapacitated by the disease.

The joint most frequently involved in a first attack is the metatarso-phalangeal articulation of the great toe, next in order being the ankles, insteps, fingers, wrists and knees. From many years' experience of seeing out-patients, now happily of the past, I should say that chiragra was more common than podagra, the explanation being that when the inflammation is in the wrist and adjacent parts the patient naturally makes his way to the hospital, whilst when the foot is involved and he is unable to walk, he finds it cheaper to call in a doctor than to incur the expense of a cab. With in-patients the condition is reversed and there are more cases of podagra than of chiragra. Cases of the chiragrous variety are common in brewers' draymen who drive the team, the nature of their occupation determining the selection of the joint involved.

It is difficult to ignore the relationship existing between traumatism and gout. The vitality of the articular cartilages and adjacent structures is lowered by the injury, and they afford a suitable nidus for the biurate which the blood is no longer capable of holding in solution. A well-known surgeon who was gouty but had had only one spontaneous attack of gout developed gouty inflammation in the wrist after carrying a small parcel of books for a lady. A subsequent attack was induced by trying to turn the stiff handle of a door. He was an enthusiastic 'cello player, but had to abandon the instrument for months together from the gouty pains it excited in the joints of the hands and arms. Such cases are by no means uncommon and endless instances might be adduced, many of them in very peculiar forms.

Amongst the curiosities of the causation of gout may be mentioned the case of a medical man, some sixty years of age, who had been gouty for many years, but who had never had a developed attack. He was operated on under ether for epithelioma of the tongue, and on the following day had a typical seizure in the great toe.

Of the ætiological causes of gout chronic lead poisoning must be taken into consideration, for lead, probably by producing interstitial nephritis, diminishes the excretion of uric acid. Lead poisoning is to a very great extent an occupation disease, but there are various ways in which it may be absorbed in small quantities. Drinking water containing gr. $\frac{1}{20}$ to the gallon is unsafe. It may not produce a blue line on the gums or any of the characteristic signs of lead poisoning, but in a gouty person it may be one of the accessory causes leading up to an acute attack. Acetate of lead given medicinally for arresting hæmorrhage, for example in piles, may act in this way, although usually a prolonged course is required. Snuff may be adulterated with lead, and many hair dyes contain it in considerable quantities.

Respecting the real nature of gout our knowledge is yet far from complete. It is generally recognised that it is connected with uric acid, but the views regarding the relationship of this body to gout are conflicting. It is easy to theorise, but in the absence of definite experimental evidence we are somewhat in the dark. Some people pin their faith to the uric acid diathesis, whilst others regard it as a myth and say that no such thing exists. Uric acid in a free state is not found in the blood, but it may be present in the form of sodium quadriurate. This salt, being an unstable body, may unite with some of the bicarbonate of sodium of the blood to form a biurate, which, if produced in larger quantities than it can retain in solution, is precipitated and deposited in the joints in a crystalline form. Gout is practically the outcome of taking too much food and not enough exercise—in other words the physiological income is in excess of the expenditure. The immediate or determining cause of an attack of gout is deficient excretion, the kidneys being primarily at fault. I remember a plethoric City man who for years had been in the habit of making a substantial breakfast, taking a light lunch, and at dinner indulging in a pint of champagne or burgundy followed by a cup of coffee and a green Chartreuse. In the evening over his pipe he had three or four glasses of whiskey and Perrier water. His health was good and there was no indication of gout. A physician whom he consulted about some trivial ailment suggested that he was taking too much alcohol, and the whiskey was knocked off, with the result that in a week the patient was laid up with an attack of acute gout, the explanation probably being that the kidneys were no longer flushed out and there was an accumulation of quadriurate in the blood. He quickly reverted to his previous bad habits and since then has enjoyed perfect health.

The term "irregular" gout is very commonly used and often without any very definite meaning. It is applied to certain distinct groups of symptoms which appear in the children of gouty parents. The most familiar of these ailments is indigestion, with its accompaniment of impaired appetite, nausea, vomiting, flatulence, heart-burn, and acid eructations. The bowels may be irregular, there may be colicky diarrhœa alternating with attacks of constipation. The patient is notably depressed, despondent, dejected, and above all irritable and hypochondriacal. In the condition known as gouty heart the patient suffers from palpitation, attacks of dyspnœa and pseudo-anginal pains. The cerebral symptoms comprise giddiness, temporary impairment of sight and hearing, and threatenings of apoplexy. There may be urinary trouble indicated by the intermittent presence of sugar in the urine, oxaluria, and even a urethritis, not of necessity traceable to infection. Gouty eczema is a well-marked variety of this affection and many cases of chronic bronchitis are attributable to this cause. That many of these symptoms are in reality gouty in origin is proved by the fact that they often all disappear on the breaking out of a paroxysm of the disease in the foot. It must not be assumed however that all these symptoms are gouty in origin. We hear a great deal about gouty iritis, gouty liver and stomach, gouty arterio-sclerosis, gouty kidney, and gouty cerebral disturbance. These phrases are the stock-in-trade of the fashionable physician, and are often but the expression of deficient clinical experience. I remember one case of "gouty eczema" undoubtedly due to scabies, and a "gouty kidney" which I should have diagnosed as a hard chancre.

"Suppressed" gout or "retrocedent" gout is another variety of which more is heard in private practice than in the course of one's hospital experience. In these cases the pain and inflammation in the joint abruptly subside with the onset of symptoms in some internal organ such as the stomach or the heart. This is regarded as an example of metastasis. When the stomach is affected the symptoms are usually nausea and vomiting, loss of appetite, and pains which are spasmodic in character. When the retrocession is to the heart dyspnœa, palpitation and even syncope may, it is said, ensue, but these conditions are certainly not of common occurrence, and are in the majority of cases readily controlled by the timely administration of a 10-gr. calomel pill.

In many people gout is incomplete in the sense that there has never been an actual developed attack. They often suffer acutely and are rarely free from strange sensations of tingling, burning, and pain in different parts of the body. A curious combination is that of the gouty with the nervous diathesis. The neuromimete usually leads an unhappy life; he feels that something is wanting and yet hardly realises what it is he requires. He is often a middle-aged bachelor who has neglected his opportunities of getting married, and finds out too late that he has made a mistake. His friends console him by telling him that having failed to make his bed he cannot expect to lie on it.

With regard to treatment, colchicum is and for many years has been the standard remedy. Respecting its mode of action little is known. It has been said that it never does any good unless given in doses sufficient to produce purgation, but this is not my experience, for small or moderate doses often prove efficacious in allaying the inflammation. The action of a large dose is readily explicable on the ground that the drug ensures the elimination of the gouty poisons by the bowels. Small doses may increase the flow of urine, but this is not always the case, and it is certain that colchicum does not increase the excretion of uric acid. In healthy people therapeutic doses of colchicum produce no symptoms save cholagogue purgation. It is not known to be of any use in any other disease than gout, with the possible exception of rheumatism, and that is more than doubtful. Ordinarily in gout I give colchicum wine in moderate doses, but in the case of the brewer's draymen suffering from chiragra to whom reference has been made I commonly give it in drachm doses with half a drachm of iodide of potassium every four hours for twenty-four hours. I do not defend the prescription, it is purely empirical, but it is efficacious in that particular class of individual at whom it is aimed, so that he is able to resume work in a couple of days. It produces violent purging and often vomiting, but it must be remembered that these patients are big, bulky, brawny men who are not readily affected by ordinary medicinal measures. I have often seen this treatment do good and have never known it do harm, but everything depends on the selection of the cases. The minimum fatal dose of col-

chicum wine is half an ounce. As an accessory measure I smear the hand freely with a mixture of extract of belladonna and glycerine, and after wrapping it in cotton-wool see that it is kept in a sling. When the swelling is very pronounced and the tension gives rise to great pain, painting with flexible collodion will afford immediate relief.

For a chronic case of gout I prescribe $\frac{1}{60}$ gr. of colchicine with a grain of calomel in a pilule every three or four hours according to the activity of the symptoms. As an accessory measure I order a drachm of calomel ointment to be rubbed into the abdomen every night at bed-time.

Colchicine, which is an alkaloid with an acid reaction, although comparatively little used in medicine is a most valuable remedy in doses of from $\frac{1}{100}$ to $\frac{1}{32}$ gr. It has a marked physiological action, producing in large doses motor and sensory paralysis with death from respiratory failure. Its action is curiously delayed, there being a latent period of from one to three hours. It expels the leucocytes from the circulation, collecting them in the bone-marrow and lungs. After a time they return to the peripheral circulation and it is then found that there is an increase in the white cells, especially of the polymorphonuclear variety. It is possible that in this curious action may be found a clue to its beneficial action in gout. Colchicine sometimes increases the flow of urine slightly, but it has been known to produce anuria of many hours' duration. "Colchi-sal" is colchicine salicylate, and is given in doses of $\frac{1}{60}$ gr. It is soluble in water.

It is doubtful if iodide of potassium is of any value in the treatment of gout, although it may be of use in the chronic inflammatory thickenings of the fibrous tissue to which that disease gives rise. It bears the same relationship to gout that it does to syphilis; it does no good in the disease itself but is useful in the sequelæ.

Lithium in the form of the carbonate and citrate are popular remedies for gout, but they are of doubtful efficacy, at all events in ordinary medicinal doses. They are excreted by the kidneys, it is true, but they exert no greater diuretic effect than would be produced by an equal quantity of common salt. They act as solvents for uric acid, but only in such a degree of concentration as would produce toxic symptoms such as nausea, vomiting and diarrhœa. It may be safely said that lithia is of no value in the treatment of gout. Lithia water probably owes any virtues it may possess to its action as water rather than to the small dose of lithia it contains

Piperazine had at one time some kind of reputation in the treatment of gout, or rather of goutiness, but that reputation has not been maintained. It is true that it dissolves twelve times as much uric acid as carbonate of lithium, but it would be impossible to get enough into the patient to exert any beneficial solvent action. It is essentially a test-tube remedy.

Sulphonal, trional, tetronal and veronal are often recommended for inducing sleep in cases of acute gout, but I have seen so many cases of chronic poisoning from the use of the "als" that I regard them all with the utmost suspicion. There is always the danger of inducing hæmatoporphyrinuria, and when this occurs the prognosis is distinctly bad.

For chronic gouty bronchitis the remedies on which I chiefly rely are pure terebene in 10-minin doses three times a day, and pix liquidum, two grains, made with lycopodium into a pill, of which two should be taken every four hours. When the asthmatic condition is the prominent symptom cubebs cigarettes will be found useful.

Gouty patients often suffer from profuse perspiration, not at the time of the attack but chronically, and for this picrotoxin, the neutral principle obtained from *Animirta paniculata*, is an infallible remedy. In the case of a man who for many years parted his hair with a towel, the sweating about the head was so profuse that when he lifted his hat he was subjected to a veritable shower-bath. A pilule of $\frac{1}{60}$ gr. of picrotoxin twice a day for a fortnight checked the distressing symptom, from which he has now been entirely free for six months. Picrotoxin is a very reliable and certain remedy for nearly all forms of sweating.

Hot baths are undoubtedly useful in many forms of gout, especially when the joints are chronically affected. To the ordinary full-length bath containing thirty gallons may be added half an ounce of pure terebene and ten drops of either pumilio pine oil or oil of the *Eucalyptus maculata*. An alkaline bath may be made with four ounces of bicarbonate of sodium and ten drops of oil of bergamot. A salt bath is prepared with six pounds of bay salt and a couple of drachms of bay rum. In cases of emergency a saline bath may be made

by pouring in a couple of bottles of any of the ordinary saline purgative waters. Sanitas, mustard, twenty ounces of the meal, and liquor ammoniæ, four ounces or more, are also useful, and common washing soda is often prescribed under various fancy names.

Dry heat gives relief, and may be conveniently applied to the affected joint by standing or sitting in front of an anthracite stove of the Salamander variety.

The dieting of the patient suffering from an acute attack of gout presents no difficulty, for he will be abundantly satisfied with three pints of milk a day and plenty of mineral water. To draw up an appropriate menu for a man who is gouty but who is not suffering from a paroxysm of the disease presents a much less easy task. He must be well fed or he will soon run down, and yet it is useless giving him food which he cannot assimilate. The best plan is to knock off joints altogether. It is true that they form the staple commodity of English cooking, but with a little care and a display of some irritability of temper their place may be taken by something more appetising and less likely to cause dyspepsia. Everything of course depends on season, but something eatable may be obtained nearly all the year round. For example, it might be well to begin with half a dozen oysters followed by consommé bortsh or bisque d'Ecrevisse. This, with a little parfait de foie gras, a snipe or woodcock and a couple of marrow bones will form a light and inexpensive repast. People always forget that the joint is the most expensive item in a dinner. A vegetable entrée is a useful institution, and a Friday without meat day has much to recommend it. In many of the English health resorts in addition to the table d'hôte dinner there is a "cure" dinner, which is usually nauseous, and is evidently designed by a person destitute of taste. The difficulty of course is about the cook. If the daughters of professional men, instead of being taught to play the pianoforte were brought up to a course of practical cookery, their fathers would live longer and they themselves would have a better chance of securing appreciative if gouty husbands. It is more profitable to feed the beast than to play to him.

Some people are infatuated with the idea of a purin-free diet. A friend of mine, who at the time was mayor of ——, consulted a physician, who drew up the following diet-chart for his guidance:

Breakfast.—Nil.

Lunch (12.30 to 1).—Green vegetables, baked potatoes and butter. Stewed figs, half a pint of junket, and 2 ounces of grated pine kernels with cream (whipped).

Dinner (7.0 or 7.30).—Biscuits, batter, 1 ounce of grated cheese or curd. Light pudding. Cream, and stewed fruit.

The patient's remarks will not bear reproduction.

There is always a great deal of discussion about the best form of alcoholic drink for a gouty man. It is useless urging total abstinence in the case of a patient who has been perhaps a somewhat immoderate moderate drinker all his life. He will acquiesce in moderation but will kick at deprivation. The best drink for a person of this description is whiskey well diluted, always supposing that he knows the difference between whiskey and silent spirit. The whiskey should be taken at meals only, and at night. He should be an abstainer between meals, not merely between drinks. The only wine admissible is one glass of port after dinner, and that rarely does any harm.

The choice of a table water is a matter of the greatest importance to the gouty or potentially gouty. It is a subject on which most people are profoundly ignorant. To begin with they do not know the difference between a natural aërated water and one made artificially effervescing by the introduction of chemically prepared carbonic acid gas. They hardly know the meaning of the word "mineralisation," and are equally indifferent to organic contamination. A gouty person should always select a natural carbonic acid water of low mineralisation so that his may be *cure de diurèse*. Of the two most popular table waters used in this country one contains of total solid constituent from 35·8 to 37·4 grammes in the 10 litres, whilst the other contains only 3·81 grammes in the same quantity. The intelligent physician will have no difficulty in advising his gouty patients which of these should be selected.

In the case of many middle-aged men in affluent circumstances it is difficult to get them to moderate their appetites and regulate their diet, but they will often accede to the suggestion of taking more exercise. For them motoring is good, but a long walk in the country every Sunday is better still, and will do much to keep down their gouty proclivities. Exercise in a close and stuffy gymnasium is irksome and monotonous, and is soon abandoned after the not inconsiderable fee for the "course" has been paid.

May 17th, 1909.

A SURGICAL CONSULTATION AT ST. BARTHOLOMEW'S HOSPITAL.

Mr. HARRISON CRIPPS: This is a boy, æt 4½ years. Last November he had a stoppage of urine—I do not think it was for very long—and that was followed by a copious hæmorrhage from the urethra. He then appears to have been well, and nothing obvious happened until about three weeks ago, when he had another similar attack, a fairly sharp hæmorrhage, and since that time he has been in the hospital. The hæmorrhage cleared up after two or three days. At the time he came in he had a slightly raised temperature, and he also had an attack of impetigo contagiosa, which is sometimes associated with a raised temperature. I examined him a day or two after he came in, but not very thoroughly because the abdomen was tender and there was this rash over it, but at that time I did not notice anything special in the abdomen. However, I examined him again a few days ago, when I could feel an obvious swelling on the left side. It gave me the impression that it might be a kidney, and I bring him here to ask the opinion of my colleagues as to what this lump may be. I have not seen this patient for three or four days, and in that interval a good deal of distension has come on. We have a skiagram here, and Dr. Walsham, who took the skiagram, has pointed out what he thinks is an internal swelling. With regard to the radiograph, of course it is easy for all of us to see anything wrong with the bones when they are photographed in that way, but I confess, from a limited amount of experience, that it is difficult for me to say whether there is anything like a tumour, in other words I think the soft parts naturally show very badly. It looks to me like a London fog in that region. But there is one important point in the photograph which I think Dr. Walsham was satisfied about—that there is something running lengthwise down the abdominal cavity. He said the long shadow is the descending colon, and the supposed tumour is lying behind it. That is important because of the possibility of this being the spleen. If it was, the spleen would probably be in front, not behind. From the history of the case and the examination of it a few days ago when the abdomen was less distended I am confident there is a swelling of considerable size in the neighbourhood of the spleen or the kidney, and seeing that he has had those two hæmorrhages I think that makes it fairly clear that it is kidney. With regard to the probable nature of it, these tumours in children often turn out to be sarcomatous, and I suspect that this child has a sarcomatous growth involving the kidney on the left side. With regard to the treatment of sarcoma of the kidney in children, operation for these cases is most unsatisfactory. I cannot say that I have ever known a case which has permanently recovered from the disease; there is always a quick recurrence. However, notwithstanding that, my own feeling would be, with the support of my colleagues, that it would be right to examine this swelling, and even if it should be sarcoma to see whether it could be removed. If it should be found to be adherent or bound down by recent inflammation so as to necessitate a severe operation, I might be satisfied with doing nothing. Still, mechanically it seems reasonably possible to remove it, and I would advise the attempt. I would not, however, urge the operation very much.

Mr. BUTLIN: One notices that the boy looks very pale; he has no symptoms of stone. The tumour seems to be on the left side, and I agree that it is probably sarcoma. I think that under the circumstances it is justifiable to explore. Some cases of sarcoma in children have cleared up satisfactorily after operation—cases in which the child has not only recovered from the operation but has remained well for a certain number of years. So I certainly think it is right to operate.

Mr. BOWLBY: I confess to feeling a certain amount of diffidence as to the presence of a definite tumour in that child. The fact that the abdomen is flatulent and distended militates against successfully feeling anything very definitely. I cannot feel a tumour at the present time. If there is an obvious swelling to be felt when the bowels are empty and the child is under an anæsthetic I think it would be right to explore, to see what the swelling is. But in the event of there being no tumour perceptible when the child is under an anæsthetic after the bowels have been emptied, the question will arise whether there is bleeding from his kidneys owing to his being a bleeder. I do not think there can be any inflammatory disease of the kidney in

the nature of tubercle, because I gather that the urine is clear, and contains no albumen and no pus and no other abnormal constituents. So I think the question of operation must be deferred until there has been a careful examination under an anæsthetic and when the bowels have been emptied.

Mr. LOCKWOOD: I think the tumour will be felt again when the abdomen is empty and the child is under an anæsthetic. Should that be so, I agree with Mr. Butlin that it should be explored and dealt with according to what is found at the time.

Mr. D'ARCY POWER: I agree you want to do something more. The bowels should be emptied and an anæsthetic given, and if you can still feel the tumour you should operate. I do not think the prognosis after operation for sarcoma of the kidney is necessarily very bad. I have operated on two or three cases of the kind which did well, and the patients were well five or six years afterwards.

Mr. WARING: I could not feel a definite tumour on account of the distension of the abdomen and rigidity of the walls. I should have the alimentary canal well emptied and the patient anæsthetised, and if on examination you can then feel the tumour in the left renal region I should do as you suggest—open the abdomen on the left side and remove it. I suppose it is most probable that the nature of the tumour is sarcoma, with muscular elements. With regard to prognosis, I do not think the prognosis in these cases is quite so bad as Mr. Cripps thinks. I have seen more than one case which has gone on for several years after the operation. If, when the patient has been anæsthetised, there is nothing abnormal to be found in the lumbar region, I think you might use a small cystoscope and examine the interior of the bladder, to ascertain whether there is anything there which might be the cause of hæmaturia.

Mr. MCADAM ECCLES: I doubt whether a tumour is to be felt in the left loin now, though there is no doubt that if the bowels were emptied thoroughly of flatus evidence of one might be found. If there is a tumour I should think, from the history, that it is probably a renal tumour, and probably of the nature of sarcoma. These cases of sarcoma of the kidney, if they are of congenital origin, are not usually so disastrous after operation as are renal sarcomata in later life. If a swelling is found I should certainly explore, and if it is safe to remove it I should do so, because these tumours inevitably tend to cause death fairly soon if left alone.

Mr. BAILEY: I believed I could feel a swelling, but owing to the condition of the child's abdomen it is difficult to express an opinion as to its nature. I should put the child under an anæsthetic, and if the tumour could be felt then I should explore, and if removable I should take it away.

Mr. RAWLING: I agree with what has been said.

Mr. GASK: I thought there was possibly some other explanation, and as the child has also leucocytosis and a temperature I should suspect the presence of some inflammatory condition there. I should examine for micro-organisms, and explore the condition by means of a lumbar incision.

Mr. CRIPPS: I shall do as has been suggested, but my preference will be to explore it through the abdomen as a safer and easier operation. But that of course is a mere matter of detail, according to individual experience.

WOMAN WITH GREAT SWELLING OF RIGHT ARM.

Mr. BOWLBY: This woman has great swelling of the right arm. There is very little to be said about her, because I brought her in to consultation a little while ago, and said then almost all I had to say about her. It was that this patient was a nurse, and without any obvious cause three months ago this right arm began to swell, and four or five weeks ago the swelling was most noticeable in the upper and outer part of the arm, and extended down to the level of the lower third of the forearm. The hand at that time was not œdematous. She had pain and the swelling extended and increased. She was kept in bed, with the arm elevated, and massage was employed. Then bandaging was done, but in spite of all that the œdema continued and extended. We have discovered nothing in the thorax or the neck, or axilla, or breast, or

anywhere else in the body, and the blood-counts showed nothing abnormal, nor was the temperature altered. She has never been out of this country. She left the hospital for a few weeks, and during her absence the œdema has markedly extended. There is now a very extensive mottling of the skin, evidently from the arrest of the stream of blood in the veins, and this condition of solid œdema without that alteration in the texture of the skin, such as one sees where there is a pure lymphatic obstruction. For where there is lymphatic obstruction alone there is an alteration in the texture of the skin, which has been compared to the rind of an orange. Since she left the hospital the arm has been treated by drainage and the insertion of Southey's tubes, and a considerable quantity of serous fluid, amounting to pints, has been taken from the arm. In spite of that the œdema has re-asserted itself. Her occupation is that of a masseuse, and her work involves a great deal of use of this arm. She first noticed the swelling, she said, a few days after pulling down a window which was very stiff and strained the arm. Nothing wrong has been discovered in the chest. There can be no question that the arm is now a good deal worse, and I notice that the patient is now really ill, and while she has been away from the hospital it has been suggested to her that the arm should be amputated at the shoulder-joint. But I suggest that we might try the passing under the skin of portions of silk by the method suggested by Mr. Sampson Handley as suitable for draining a certain number of œdematous limbs of their fluid. I admit that if this does not succeed she must probably lose the arm. As to the causation of the trouble we are in the dark. Previously when I brought her here people asked whether the patient had tied anything round the limb, and whether she had been in the habit of trying to make it swell by artificial means. With this idea she was carefully watched in the ward, but nothing was discovered. I do not think the causation of swelling is to be thus explained, and I shall be glad to hear suggestions as to treatment.

Mr. Butlin: I think that in order for there to be such obstruction as this there must be some gross lesion, affecting the veins and the lymphatics. Mere pressure on a vessel from outside is not sufficient to cause such a limb as that, and if there were a gross lesion it should be palpable, but there is no palpable lesion. It is worse than most of the conditions of elephantiasis which one sees in connection with cancer of the breast. So I cannot help having a suspicion that she may have produced it by some means, and yet I cannot understand that any pressure which she could have made with the hand would be sufficient to produce such a condition as this. I agree that treatment by Mr. Sampson Handley's method might be tried, and it will be time when you see whether that succeeds or not to think about amputation of the limb.

Mr. Cripps: I was not here when the patient was shown on the last occasion, and I am interested in the possibility that it may be factitious, because one sees from time to time conditions of the limbs which have been produced by something tight tied on to them. Two or three of these we have had shown in this consulting room, but they never had the appearance of this case; they were merely soft œdema. This is very much beyond anything I have seen produced in an artificial way. So I do not think that is the cause. I associate the condition with a straining of the arm she had shortly before noticing the swelling. I think she has some injury or occlusion of the brachial vein or veins, or possibly the artery. There might be some traumatic aneurysm. The limb seems harder than it would be if there were simple venous obstruction alone. I think there must have been some leakage of blood. With regard to the treatment, I do not think any harm will be done by allowing a short delay while drainage is practised. If that does not succeed I should be inclined to cut down carefully over the swelling with the view to exploration, and if nothing was found that could be remedied an amputation might be necessary; the exploratory incision could be made the first stage in the amputation. But I would look well into it first of all before actually amputating.

Mr. Lockwood: It is obvious that the patient is now acutely ill. Her pulse is 112 to 120, so it is clear that the case must be taken in hand soon. The impression on my mind is that there is accumulation of blood-clot, and, as Mr. Cripps suggests, it is in the upper part of the limb. I would advise that an incision be made, and that that point be cleared up as a preliminary. I think probably the skin will give way, it is so tight.

Mr. D'Arcy Power: I saw the case before, and she is materially worse now. The swelling has extended upwards, and I think you are bound to explore there.

Mr. Waring: I remember discussing the question on a former occasion whether she had put something round the arm. I take it that you are now satisfied that this explanation has been excluded. The affection has a very marked line of demarcation above, and I think that some form of constriction may still be part of the explanation of it. The œdema extends much higher up the limb than when I saw the patient previously; she now has thrombosis of the brachial vein. I should investigate through an incision in the upper part of the arm, along the course of the thrombosed vein.

Mr. McAdam Eccles: When the case was shown last time the swelling was so markedly on the outer side of the upper arm, near where the scar is, that several of us thought it might be due to inflammatory mischief in connection with the bone. And I think still there is a possibility that she had some inflammatory condition there which has spread round and involved both vein and artery. The point as to its being possibly self-induced is still worth considering, because I have known the patient and have seen her once or twice before she came to the Hospital, and I have no doubt she is the type of person who might do this. But I feel that we ought to try to get a re-establishment of the circulation, both venous and lymphatic, but I am doubtful whether it will be of use; I fear the limb will in the end have to be amputated.

Mr. Rawling: I agree that you ought to try Mr. Sampson Handley's method of drainage in this case, though I admit I do not feel hopeful about it; I think you may have to do amputation, and, from the condition of the tissues, it is possible that the scapula may require removal as well.

Mr. Gask: I think the right thing will be to explore first, and be guided by what you find.

Mr. Bowlby: I shall operate upon that to-morrow. The reason I did not operate before was that she made up her mind to try somewhere else, and she went out before I had the opportunity.

Enlarged Glands in the Neck.

Mr. Bruce Clarke: This patient has enlarged glands in her neck, and I will give you a brief history of her case before she comes into the theatre. The glands were first noticed in January, 1905. She had them completely removed at the Sussex County Hospital in June, 1906. Another operation was done in June, 1907, and she had another operation in June, 1908. You will see now what her condition is. I have been informed that a skiagram has been taken of her neck, and that there is something peculiar about the second cervical vertebra. I do not think I can say anything more about it than that there is something peculiar. I do not think it warrants my saying at present that there is a disease of the vertebra. It may be that there is some calcareous deposit in the growth. I cannot say I look very hopefully upon the case, although I have no record of what the nature of the disease in her glands, which were removed, was. Probably, however, they were lympho-sarcoma. But the way in which they have gone on increasing since last June seems to make it impossible, whatever the nature of the disease and whether the seventh cervical vertebra is diseased or not, to remove the glands satisfactorily. She has lost a good deal of flesh, and there is a softened spot on the surface, where there may be local suppuration, and the pus there may require to be let out. There are glands behind the sternum, glands in the axilla, and I do not think it is possible to do any operation to satisfactorily relieve her. It seems to be a case in which one may very fairly try the new brand of Coley's fluid, which is being employed at the hospital now. I have one patient who is undergoing that method of treatment, and I think with some success, though it is yet early to speak definitely on that matter. The new Coley's fluid seems to be better than the old. I have a patient who is under it now, but who has only been having it a short time. The swelling, which is on the side of the head, is diminishing, but to speak further about it would be premature.

Mr. Butlin: I think that patient is a typical example of the hard form of lymphadenoma or Hodgkin's disease. I do not think there is pus in the red spot in the swelling. I agree that it is a hopeless case as far as operation is concerned. I

had one or two cases in the hospital five or six years ago, and gave them arsenic, on which they improved to some extent; the arsenic was pressed until it caused arsenical neuritis. In some of the patients the glands grew smaller, but the patients died. I have never seen a case of this disease recover. One method of treatment proposed for these cases is by X rays, and the other is by radium. I see occasionally in the 'Centralblatt' records of cases cured by X rays, and I should myself much like to see a case of this disease cured by X rays or by any other treatment. I look upon such a case as absolutely hopeless.

Mr. CRIPPS: I take the same view with regard to the diagnosis of it. And operation I also agree is out of the question. So far as trying these remedies which have been mentioned is concerned, during the last thirty years which I have spent in the hospital there has never been a time when there was not a new remedy for curing malignant disease, but I have yet to see any of them successful.

Mr. BOWLBY: I regard the case as hopeless.

Mr. LOCKWOOD: I suggest that those glands might be removed for examination; it would not do any harm. And afterwards I should employ the method of treatment in which you had most faith—Coley's fluid, I think.

Mr. D'ARCY POWER: Because it is hopeless I should try some of these organic compounds which have been referred to.

Mr. WARING: This is a very extensive case of lympho-sarcoma and I do not think it is possible to remove the entire disease by operation with success. I see no objection to treating it with Coley's fluid. I have seen it tried in some cases, but usually with unsatisfactory results. I suggest you should take out one of the enlarged lymphatic glands and examine it histologically, in order to determine the exact nature of the disease, before commencing the injections of Coley's fluid.

Mr. RAWLING: I agree that it is a bad case of lymphadenoma, and that it is hopeless from an operative point of view. With regard to Coley's fluid, I think it is a waste of time to use it. The results obtained have been most unsatisfactory. I think Mr. Butlin has used it a good deal, but I believe I am correct in stating that he has not had much success with it.

Mr. BUTLIN: No; but since I tried it it has been altered, and the last reports of it have been better in many ways. I think there are cases which appear to be cases of new growth, and the structure is that of round-celled or even of spindle-celled sarcoma, and yet they are not really malignant growths. At present there is no means of diagnosing such cases; but I have a suspicion that they are sometimes cured by the use of such means as Coley's fluid. And I should therefore recommend the use of Coley's fluid in cases of round- and spindle-celled sarcoma in the hope that the disease would now and then clear up under it.

Mr. GASK: I would remove a piece of that growth for diagnosis.

Mr. BRUCE CLARKE: I will remove a piece for diagnosis, and then we shall see where we are. I have had enough suggestions for treatment to last me for some time.

HEERMANN reports success in treatment of heart and lung affections by applying heat to the legs to draw the blood away from the congested area. It was wonderful to see the improvement in extreme cyanosis with failing cardiac compensation, no effect being obtained from digitalis; all the symptoms of congestion subsided in a few minutes after the hot-air apparatus had been applied to the lower part of the body. Local application of heat to the heart has the same effect in rheumatic troubles as application of heat to the joints. He now applies local heat to the heart in all rheumatic affections once or twice a day for from ten to forty-five minutes at a time. In no instance has there been the least intolerance on the part of the heart, and the relief was so marked that the patients clamoured for it. The ice-bag should not be used until local heat has been given a trial, as it is impossible to determine beforehand the cases in which cold or hot applications will give most relief.—*Journ. A. M. A.*, vol. lii, No. 18.

DR. A. F. TREDGOLD
ON
CRIMINAL RESPONSIBILITY OF AMENTS.

THE law of England recognises that persons suffering from certain forms of mental disease cannot be held accountable for their actions, and generally speaking this is the case with idiots and pronounced imbeciles, or any person who, in the words of Mr. Justice Tracey, knows what he is doing "no more than an infant, a brute, or a wild beast." With regard to the milder degrees of defect, however, the mere presence of feeble-mindedness does not of necessity absolve a person from the consequences of his acts, and the criminal responsibility of such persons, as well as of the insane, is by no means clearly defined. There are certain precedents and rulings which are usually followed in such cases, but in any particular instance the fact of the responsibility or otherwise of the accused is a question for the jury to decide upon the evidence presented to them. Criminal offences in which this question of responsibility is raised are exceedingly common, and it is plainly the duty of the members of our profession, who alone can form a correct estimate as to the extent to which conduct is likely to be influenced by mental deficiency or disease, to formulate general principles, and to give their opinion regarding the mental condition of any particular accused person in order that the jury may arrive at this decision. These general principles, however, must be just, and whilst protecting those who are really irresponsible from undeserved punishment, they must also protect society against the escape from punishment of those who, even if mentally deficient, are rightly accountable for their actions. The rulings of English courts at the present time are generally based upon the replies of the fifteen Judges to the House of Lords in the middle of the last century. Briefly, it may be stated that for an accused person to be held irresponsible on the ground of insanity, it must be shown that he was of diseased mind, and that at the time he committed the act he was not conscious of right or wrong, or was under some delusion which made him regard the act as right. This dictum, it will be observed, takes no account of the question of defective control, an omission which was pointed out in the exhaustive treatise of Sir FitzJames Stephen. According to this eminent jurist, "No act is a crime if the person who does it is, at the time when it is done, *prevented from controlling his own conduct*, unless the absence of the power of control has been produced by his own default." I do not propose to enter into any discussion regarding the diminution of the will in ordinary persons or even in insanity; but I am quite certain that in persons suffering from amentia a diminished power of control is so commonly present, and such an essential part of their mental condition, that a grave injustice may be done if this be not taken into account. There *may* be non-defective persons who, whilst fully appreciating the nature and consequences of certain criminal acts, are yet incapable of refraining from committing them, and such cases are described as impulsive insanity. But it cannot be doubted that there *are* aments who suffer from a definite defect of control which leads them to commit criminal acts. I would therefore say that, whilst the mentally deficient person is not necessarily irresponsible for any crime he may commit, he should certainly be held unaccountable when he commits an act (1) of which he does not understand the nature or that it is contrary to law; (2) which is the result of an impulse he was unable to control; (3) which is the natural result of a delusion of which he is shown to be the subject.

The above is taken from Dr. Tredgold's book on 'Mental Deficiency' published by Messrs. Baillière, Tindall and Cox, 8, Henrietta Street, Covent Garden, London. The author dedicates his interesting volume to all those persons of sound mind who are interested in the welfare of their less fortunate fellow creatures, and this indicates very well the trend of this remarkable and valuable work. The luminous statement of the author in regard to the difficult question of the criminal responsibility of aments affords an excellent example of the lucid manner in which the book is written, and the wealth of illustrative cases which are to be found in its pages render the publication an admirable exposition of one of the most difficult fields of study in medical science. During the past few years the subject of mental deficiency has evoked a large amount of attention from many prominent persons interested in social and philanthropic questions. To members of the medical profession in particular it is one of much importance, on account of their responsible duties connected with its diagnosis, with the treatment and training of these patients, and their examination and certification as to fitness for special classes and schools, training-homes, and asylums. And there is no doubt that with new legislation, which cannot now long be delayed, these duties and responsibilities will be considerably increased.

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A CLINICAL LECTURE

ON

EMPYEMA.

Delivered at Guy's Hospital.

By W. HALE WHITE, M.D., F.R.C.P.,
Physician to the Hospital.

GENTLEMEN,—We will take to-day the case of the patient whom you see sitting before you. She is a woman, æt. 34 years, who came into the hospital on September 30th under my care in Mary Ward. The history is that she came in for cough, pyrexia, and shivering. Towards the end of August she caught a cold, but the present illness began with a pain in the right side of the chest on Friday, September 18th, with shivering. A doctor whom she consulted said she had pneumonia. When she came in we found that the left side of the chest moved well, but the right side moved badly. We found in both sides of the chest a good many rhonchi, and on examining her carefully we found that she was dull and had signs indicative of there being a collection of fluid beneath the area which I am marking out on her body. In other words, it was on the right side of the chest, about the second, third, and fourth ribs, between the sternum and the anterior axillary line, as shown by the dark area in the X-ray picture which I put before you. The expectoration was purulent, so much so that we had no doubt that she was coughing up pus. And bearing in mind that she had had pneumonia before she came in, there appeared to be very little doubt that she was an example of an empyema following pneumonia, which empyema had ruptured into one of the bronchi. She really was, as she will tell you, very ill. You will see from the temperature charts that when she came in her evening temperature was 103° F. for the first fortnight. It is a typical hectic temperature, with a raised temperature in the evening and a lower

temperature in the morning. Having made this diagnosis the next thing was what to do with her. And what we have done with her was to put her to sleep on the balcony, where she spent the whole of the days and nights ever since she came in. She has there had the open-air treatment. In the next place we got Dr. Eyre to cultivate some micro-organisms from her expectoration, and he found that it contained the *Bacillus coli* and the pneumococcus, and the *Staphylococcus aureus*. Then the blood was examined in order to ascertain its opsonic index to these micro-organisms, and it was found that the index to the *Bacillus coli* was 0·43, of the *Staphylococcus aureus* 1·04, and of the pneumococcus 2·42. It was clear that the lowest opsonic index was that of the *Bacillus coli*. Accordingly Dr. Eyre prepared a vaccine from the *Bacillus coli* recovered from the patient, and several injections of that have been given. The first dose was two millions on October 10th, a small dose on October 17th, and subsequent doses on October 29th, and one on November 21st. So you see the treatment has been summed up in putting her out in the open air, and vaccinating her against the micro-organism which was present in the blood and gave the lowest opsonic index.

You will naturally want to know whether that treatment has been successful. That it has been successful I can prove to you. In the first place if you doubt it you can ask the woman herself; she is very eloquent of the improvement which followed the treatment. After the first week of the treatment the temperature had fallen, in the second week it fell a little lower, and in the third week still lower. In the fourth week it had become normal and remained so through the whole week, and the same is true of the fifth and sixth weeks. Not only that, but she has gained very considerably in weight, namely over 7 lb., during the time she has been under treatment. Further, her physical signs have improved, and although over a considerable area her chest was previously dull, you can hear now when I percuss her chest that there is not much abnormal. The breath-sounds are also normal. I should have liked to have shown you an X-ray photograph to-day showing the improvement, but the prints are not ready. (They showed that the previous very dark area was much lighter.) So we have had in this woman a case of empyema discharging into the lung, and you have seen the improvement under a certain plan of treatment. This afternoon I propose to go over with you some points in connection with the treatment of empyemata. When you are brought face to face with an empyema which is being coughed up, the first thing you have to say to yourself is, Is this empyema producing such a severe general infection that the patient is dying from pyæmia? That may occur. I have notes here of a girl, æt. about 16 years, who had pneumonia, who had empyema which had ruptured into the lung, and she coughed up a quantity of pus. This pus stank so that it required some resolution to go into her bedroom. I put a needle into the chest in many places but I failed to find pus. Nor, as I have often told you in the wards, was I surprised at this, because the child was coughing up pus so fast that it never collected, and I could not hope to find any. She had diarrhœa, she had profuse sweats, she was very pale, she was losing flesh rapidly, she had a marked hectic temperature, and it was clear she was going downhill. I therefore gave her a good large dose of morphia subcutaneously one evening, and that stopped her coughing. Consequently the pus collected, the next morning I again went over the chest and put a needle in where the physical signs seemed to indicate fluid, and I succeeded in drawing off the pus. Sir Alfred Fripp resected a rib, put in a drainage-tube, and the patient completely recovered. That is therefore an example of a case of empyema discharging through the lungs in which the septic symptoms are so severe that something must be done at once in the way of draining in order to save the patient's life. But you would not expect septic symptoms to be very severe with empyemata which are being coughed up, because the pus is discharging externally, and, as a rule, when pus from an abscess is discharging externally there are not severe symptoms of general infection. So now I will give you instances of cases in which there were no immediately dangerous septic symptoms as a result of empyema which was being coughed up. I have already shown you one case, that of our present patient, and here are notes of others. But before giving you them I may remind you that I find from talking to people that there is a general impression that these cases of empyema which are being coughed up should always be drained.

But you see from this woman's case that they can get well without any surgical operation at all, and there are many reasons why you should not drain them unless they have such severe septic symptoms that they are dying from them. For example, it is often difficult to find the pus; we have not even needled this woman, because I thought she would get well without operation. It would have been difficult to find the pus if we had, because she was constantly emptying her cavity of of pus. You do not find pus with the needle because it is not there. You may be unable to stop the cough for sufficiently long to get enough pus collected in the cavity for you to find it. Another point is that although the X rays will often help you very much, if the pus is surrounded by a large mass of thickened pleura, it may, even with the help of an X-ray picture, be difficult to find the pus, although it is somewhere in the centre of the dark shadow. I do not suppose that in our patient the pus-containing cavity was as large as the dark area in this skiagram. Again, if you let the pus collect by giving morphia you still may not be able to hit it off with the needle. Another thing to bear in mind is, that empyemata surgically treated do not uniformly do well. That is brought home to us at present in John Ward. We have had to send out one child in whom the empyema has not healed, although the operation was done weeks ago. And there is a child at present who has been operated upon twice for its empyema. It is months since the first operation and it is not well yet. So although the wound may heal quick after an operation for empyema, often it does not, and the patient is then in a deplorable condition. I have known two or three cases in which the patient has died from lardaceous disease owing to the constant suppuration of an empyema which has been opened. If the lung does not come forward to fill up the space you are liable to get a chronic pus-containing cavity leading to lardaceous disease. Many years ago, before empyemata were opened as skilfully as they are to-day, a much larger number were coughed up than is now the case and many of them recovered.

But to return to my notes; I have here notes of several cases in which the empyema has been coughed up and the patient has got quite well without recourse to an operation. In the first of these a woman had empyema following upon pneumonia. Her temperature was hectic, but fluctuated considerably. A few days after I saw her she coughed up a quantity of pus, and ultimately got perfectly well. In another case, a boy had been in Great Ormond Street Children's Hospital, where they could not quite decide what was the matter with him. After he left that institution he coughed up a quantity of pus and got quite well. No doubt he had an empyema. A further case is that of a young man, who was taken ill with pneumonia in June, 1901, coughed up pus in July, was sent to winter in Falmouth, and the expectoration ceased. In the spring he was quite well. In June, 1902, however, he again coughed up pus, but the empyema could not be found by the physical signs. He went again to Falmouth, coughed up more pus, and became quite well. In a communication that I had with him previous to this lecture he stated that he is still in excellent health, and able to run a mile as quickly as most people. A similar case is that of a woman who, although three years have passed since her illness, is still perfectly well, and has no expectoration whatever. I have the notes of a case of a man, æt. 60 years, who was subjected to repeated needling without the empyema being found. He was sent to the seaside, coughed up pus, and got well. That took place two years ago and he has had no recurrence. I have seen many other cases of empyema in which the septic symptoms were not sufficiently severe to make it necessary to operate at once, and which perfectly recovered by being sent into the fresh air and allowed to cough up the empyema.

It may be asked, Have you had no cases of failure? Yes; during the time covered by these cases three people who had been left to cough up their pus have died. One of these cases was that of a woman, well over sixty, and an exceedingly unhealthy subject. She looked as if she weighed sixteen stones. There were signs of fluid at one base, and she had a hectic temperature, and was coughing up pus. We could not find the empyema by needling anywhere, but did not operate, for she was so unhealthy that it was difficult to believe that she could survive an operation. This patient died ten days after I saw her. Another case was that of a big, elderly man, also very unhealthy looking, who had an empyema at one base, some pneumonia at the other, and was coughing up pus. We decided that any operation would probably be

fatal. He was therefore left alone, and died within twelve hours of being seen. If any of my audience had seen these big, unfavourable subjects they would not have dreamed of operating. A third case of death resulting from an unopened empyema with purulent expectoration was doing well when a sudden hæmorrhage supervened. There was no post-mortem examination, but it is to be supposed that some vessel became eroded in the empyema cavity, and that the loss of blood resulted in death. But this would have been just as likely to occur whether the empyema had been opened or not. One may therefore conclude that in many cases people who have not been operated on do very well indeed. Of the three cases in which death resulted upon being left alone one was due to a pure accident, and the other two belonged to a class of case that could hardly have survived any operation.

The next point to be noted in the patient the subject of this lecture is the efficacy of vaccination. When we have to deal with pus-discharging cavities which are slow of healing, it is advisable to vaccinate the patient against the micro-organism. Fresh air and vaccine together make an excellent form of treatment. One case I remember was that of an old man, mentally weak, who had had pneumonia and developed an empyema at the left base. He was coughing up pus. A more unsuitable case for operation it would be impossible to imagine. We accordingly vaccinated him, and after vaccination the temperature became normal. It is nine months since the vaccine treatment began; within two months he was quite well, and he still remains well. The micro-organism in this case was the *Streptococcus lanceolatus*.

I may next mention the association between empyemata and general peritonitis. When one remembers that empyemata are generally due to the pneumococcus, and that general peritonitis may be due to the pneumococcus, it is not wonderful that there should be this association. Of thirty-eight cases of empyema observed in the post-mortem room during a certain period, peritonitis was present in seven. A peculiar case was that of a woman in Miriam Ward who gave a history pointing to pneumonia; there were signs of fluid at the left base, and of some fluid in the peritoneal cavity. There was no rigidity of the muscles of the abdomen. A needle was put in the dull area of the chest, and some pus was withdrawn. At the subsequent operation the pus gushed out of the empyema, and Sir Alfred Fripp, who was conducting the operation, thought, judging by the great quantity of pus, that the empyema extended far between the diaphragm and the base of the lung, but at length one of the clinical assistants remarked that all the fluid had disappeared from the abdomen, and we then found that a drainage-tube passed into the chest went easily through a large hole in the diaphragm into the abdomen. The course of events was then perfectly clear. The woman had an empyema and peritonitis. There was a perforation of the diaphragm, and the two communicated. She was vaccinated with a vaccine from the micro-organism of her own pus, and got better, but a second operation was necessary to mop out some pockets of pus in the abdomen. After that the patient got perfectly well, and can now walk several miles.

Very often mistakes are made about empyema for there is a belief that a pneumonia may be slow in clearing up, leaving the lung solid and the temperature high for some time. This is not the case. Pneumonia is a specific fever which ends on a definite day, and, almost without exception, when after pneumonia physical signs indicative of solid or fluid remain, and the temperature continues raised, this state of affairs does not indicate trouble in the lung, but empyema. Remember that an important guide to the localisation of an empyema is local tenderness. When there is uncertainty it is a good plan to push the finger against the ribs and insert the needle at the tenderest spot. To show the difficulties which may occur I may mention one extraordinary case which I had under me in the hospital. The patient was dull all down the back on the left side. Thinking there was fluid, we put a needle in at the tenth space and got some pus; then needled the ninth and eighth and found no pus. We therefore concluded that there were thick pleural adhesions down the back to the tenth rib, and an empyema at the base. The empyema was opened, and, to our surprise, large quantities of pus gushed out, and it was found that the empyema went right over the diaphragm and up in the front part of the pleural cavity to the first rib, but that it was limited laterally by adhesions in the anterior axillary line. By putting needles in at

the back above the place where we found the pus we made quite certain that the higher spaces did not contain pus at the back, but we never thought that the empyema would extend in front. Adhesions may in that way render an examination difficult. Sometimes we may imagine pus to be in the pleural cavity when it is not—when, in reality, the cause of the trouble is a growth. One case bearing on this point was a man, æt. 41 years. Many doctors who saw him said that he must have pus in his chest. He had a hectic temperature, a leucocytosis of 20,000, and all the signs of pus in the chest at the right base, or of a subphrenic abscess on the right side. In the confidence that he had an empyema he was needled in many places, but it turned out that, instead of an empyema, he had rapidly growing sarcoma of the mediastinum and of the mesenteric glands. It must be kept in mind that a rapid growth will give signs resembling those of an empyema, and if time permitted I could tell of many cases in which a growth has been confused with pus.

We know very much more about empyemata to-day than we did a few years ago. When I was a student, the text-book for this subject was the fourth edition of Bristowe's 'Theory and Practice of Medicine.' Turning to this edition the other day, I find that the author does not mention empyema as a complication of pneumonia, and, turning to empyema, he does not even give pneumonia as one of its causes. Some time ago I analysed some figures from our records here at Guy's Hospital bearing upon the relationship of empyema to pneumonia. It will be found that when pneumonia is at its greatest frequency then the proportion of cases of empyema following upon pneumonia is also at its greatest. In 1893 there were 138 cases of pneumonia, of which 4·94 per cent. were followed by empyema. In 1891 there were 108 cases, of which 5·5 per cent. were followed by empyema. Never since then has there been such a high percentage of cases of empyema following directly upon pneumonia, or so many cases of pneumonia in one year. It is very well known that when empyema follows upon pneumonia, the usual course is for the crisis of the pneumonia to occur, the temperature to fall for a day or two, then to rise again, remaining hectic—about 102° F. in the evening and 99° F. in the morning—until the empyema is either opened or discharged through the lung. One must suppose that the pneumococcus is active the whole of the time, and yet there is the crisis, the fall of the temperature, and the subsequent rise. Some cases of pneumonia have an empyema in association with them from the very beginning; in other cases the onset of a hectic temperature indicating the presence of pus may be very long delayed. One patient had the initial rigor of pneumonia on September 23rd, and it was not until November 6th—six weeks afterwards—that the temperature began to rise gradually again, until on November 12th it had reached 102° F. in the morning and 103·8° F. in the evening. Four ounces of pus were evacuated when this empyema was drained, and the patient got quite well. The quantity of pus, by the way, is curiously variable. In one case, a child, who had a characteristically hectic temperature for several days, the empyema contained only half an ounce of pus—a remarkably small amount to keep up the temperature. On the other hand, I have known 170 oz. of pus to be present in one pleural cavity. The patient was æt. 57 years, and got perfectly well. Considering the rigidity of the chest, one wonders how such an elderly man survived. In connection with this, it is worth while in passing to notice that in simple pleurisy clear fluid may be met with in large quantities. I have known clear fluid to collect in a chest at the rate of three ounces per hour, and I have proved it by emptying the chest by aspiration, taking out one hundred ounces, and at the end of thirty hours another hundred ounces. The largest amount of clear fluid I have known one pleural cavity to contain was about 220 fluid ounces.

Another strange thing about empyemata is their preference for the surface of the lung next to the chest. Interlobular empyema is very rare, and I have never seen one between the inner surface of the lung and the pericardium. With the patient lying in bed there is naturally a tendency for the empyema to take the lowest point, *i. e.* the back. I have needled at the ninth space, close up against the vertebral column, and have found an empyema there which did not extend more than two inches from the vertebral column. Double empyema is very rare. I have not looked up all my notes, but I can only call to mind two cases having this condition. In one case signs of pneumonia had been fairly evident at both bases, and at the end of ten

days there were signs of pus at both bases. The empyema on the right side was opened and drained by Sir Alfred Fripp, but if he had drained the other there and then he would probably have killed the patient. The right lung had to be allowed time to recover before opening the left chest, so five days afterwards the other empyema was emptied by means of an aspirator. The pus of course re-collected in it, so at the end of another week it was again aspirated, and a week later, the right lung having come to the surface, the left empyema was drained. The patient made a complete recovery. This case shows the method of treatment you should follow in dealing with double empyemata. If in any empyema there is a large amount of pus, do not evacuate the pus suddenly. Give the patient an anæsthetic, put in a trocar and cannula, attach a rubber tube to the cannula, and let the pus out slowly. Then after the pus has come out, with the patient still under the anæsthetic, excise a piece of rib, open the cavity in the usual way, and put in a drainage-tube. If you open a large empyema and let the pus gush out, the patient may die from sudden movement of the previously displaced heart.

I have already referred to one division of empyemata, distinguishing between those in which, although pus is being coughed up, an operation is necessary, and those in which it is not. Another important division is into those cases in which the empyema is an evidence of a septic process in the body as distinct from those which are merely local in the chest. I have seen, for instance, the other day an empyema associated with angina Ludovici, and if time permitted I could quote several instances in which an empyema was part of a general pyæmic process. When the empyema is part of a general septic process the patient is in a bad way, and although it is the surgeon's duty to open the empyema, recovery is very doubtful indeed.

A number of X-ray pictures were shown at the close of the lecture, illustrating how well the lung will recover after a quantity of pus has been coughed through it. The lung in one case had had more than fifteen gallons of pus coughed through it, and by means of open-air and vaccine treatments the patient gradually got well.

May 24th, 1909.

A CLINICAL LECTURE

ON

A CASE OF ENTERIC FEVER.

Delivered at St. Bartholomew's Hospital.

By J. A. ORMEROD, M.D., F.R.C.P.,
Physician to the Hospital.

GENTLEMEN,—The patient whom you see, a girl, has been convalescent for some weeks. The only result of the disease which you can see now is that her hair has come out a good deal. Loss of hair after acute disease is common, and particularly common after enteric fever. She is small for her age, and rather thin, though before her illness she says she was stout.

Now I am going to ask you to follow the fortunes of this girl since she has been in the Hospital. She came in on June 26th, so her stay here has been a long one. Her age is 20, she is single, and her occupation that of a cigar stripper. Her previous health was good; I cannot find that she had any particular complaint before this. Her father and mother are both alive and well. She had three cousins in Hoxton Infirmary with typhoid fever, the last one having been taken ill three weeks before this patient's admission to our Hospital. She had visited their house and seen them in the Infirmary. Did she catch the disease from them or in their house? It seems probable; but we do not know what she did there—what she may have eaten or drunk, whether she helped to nurse them or to wash their linen, and so forth. Another cousin's wife who visited that house was admitted into Hope Ward on the 19th of the previous May, so it is very probable that the house of those cousins was a focus of infection both for this case and for the case which was in Hope Ward. As regards the history of the onset, she told us she was well until June 15th, and that then she began to have cough and headache; but she continued her work for a week, though she had shivering attacks and also some diarrhœa. This diarrhœa stopped on June 22nd. She took to her bed on June 22nd, complaining of a pain in her back and sore throat, and she was admitted on June 26th. You see, we were met with the difficulty which always occurs in dating the disease. She gave us

a fairly definite date—June 15th—and at first we dated the disease from June 15th. But, looking at the later course of the disease, I should think perhaps it is more probable that we ought to date the onset from the time she went to bed, namely June 22nd. That would be in accordance with the rule which Osler gives. But often you cannot exactly say when the disease begins, for there are symptoms which you may either regard as premonitory, or as actually indicating the onset of the disease. Still, we will take June 22nd as the date of onset. On that supposition she was admitted on the fifth day of the disease complaining of pain in the loins and headache. She had the dull, heavy look which you know is so common in enteric patients. Her tongue had a thick white fur in the centre, but it was moist. Her temperature was 104° F.; pulse 128, regular, small volume, low tension; respirations 26. She had the physical signs of bronchitis, namely coarse râles all over her chest. Her heart-sounds were normal; her abdomen somewhat distended, but otherwise normal. The abdominal reflexes were present; they are often absent in typhoid, according to Dr. J. D. Rolleston. There were no rose spots, and we could not feel her spleen. We could obtain no knee-jerk. The urine was normal; the bowels were constipated, the diarrhœa having by this time stopped. An enema was given, and it was followed by one dark, firm stool. With regard to the blood-count, her white corpuscles were 13,200, so there was no lack of white corpuscles: indeed, they were rather in excess. Widal's test was not positive, only suspicious—that is to say, a dilution of 1 in 50 gave a little clumping after an hour. So as regards diagnosis by the laboratory tests, viz. Widal's reaction and the leukopenia which we look for in enteric, it was uncertain, I suppose because the disease was in quite an early stage. As to the clinical examination, there was no conclusive evidence of typhoid; for there were no rose spots, there was no enlargement of spleen, no diarrhœa, and the abdomen was not tender. Still, the history of the mode of onset, the rise of temperature without obvious cause, and the general appearance of the patient, made it probable that it was typhoid, and of course that was made still more probable by the history of the typhoid in the relatives. And it justified us in treating the case as one of typhoid. She was of course put strictly to bed, was given no solids, only milk and water, and she was ordered to have an enema as often as necessary, which meant practically every other day. She was to be cradled when the temperature reached 103° F., and sponged when the temperature reached 104° F. With regard to medicine, she was given bicarbonate of soda and peppermint water, because her abdomen was somewhat distended, and also cinnamon oil, two minims three times a day. Cinnamon oil is said, on the authority of Dr. Caiger, to reduce flatulence, and make the patients more comfortable than they otherwise would be. Not very long after admission she vomited about three times. In three days' time, viz. on June 29th, some doubtful spots appeared on the abdomen. During the next week, the second week, from June 22nd to July 5th inclusive, the temperature did not vary very much; it ranged between 102° and 105° F., pulse 108 to 116. The tongue was still thickly furred but not dry. She began to be delirious at night, and her bronchitis got worse. Cold sponging was stopped on account of the increasing bronchitis. But towards the end of this second week she had better nights though her pulse became still quicker—120. During the third week, that is to say July 6th to July 12th, the temperature continued high, the pulse still more frequent, namely 112 to 136. The bronchitis became very severe, her face became blue, and the condition of the lungs caused much anxiety. The stools were black, and she still required enemata. She was also very deaf. I dare say you know that enteric patients are often deaf. It used to be a saying amongst the older physicians that this was a good sign, because such patients always pulled through. I do not know why that should be so. However, deafness was marked in this patient and doubtless it served to accentuate the stupid state into which she now fell. For she used, at this time, to lie like a log, not moving from the position in which she was placed. Nevertheless she was more or less delirious and she refused her food, which of course was rather awkward. I think it was partly because she disliked fluids; her whole desire was for "cake." The consequence of this refusal was that she had to be fed through the nose, which is not often necessary in typhoid cases. On July 8th there was a sudden fall in temperature, which caused some temporary alarm. It came down in twelve

hours from 104·5° to 99·5° F. Seeing that the disease was in the third week, the suspicion arose that she might have a perforation or a severe hæmorrhage. On the other hand, however, her abdomen continued as before, her pulse did not vary, no blood appeared in the stools, and she did not seem generally worse. Therefore we waited on events, and no other alarming symptoms followed—indeed from that date she began to improve a little. I think the sudden fall of temperature may have indicated the beginning of the remissions which take place towards the end of the fever. For in the second half of the third week, that is to say July 5th to 11th, the temperature began to go down in the morning to 101° F, and the patient became brighter. On July 11th Widal's reaction was again tried, and this time it was quite positive. On July 12th another disagreeable symptom occurred: she passed blood *per rectum* into the bed. But this also was followed by no serious result. After July 9th some remission of the morning temperature appeared, and in the fourth week this was quite marked, the thermometer registering 99° F. in the mornings, 105° and 104° F. in the evenings. The pulse-rate was rather lower, 110 to 124 to something more sensible. She took her food again, the bowels acted without an enema, and everything went on well, except that the bronchitis did not completely clear. Now we thought we were coming to the end of the illness, and were just beginning to improve the diet, giving her an egg and a little boiled bread (for she was clamouring for food), when on July 18th the temperature began to go up again, the morning remissions ceased, the temperature ranged up to 104° F. throughout the day, the pulse was 120 to 134, and very bad volume, respirations 44, 50, and even 60. The tongue, which up to this date had been fairly good, now became dry, furred and tremulous, and she now seemed to be worse than she had been yet. The bronchitis was as bad as ever, she was deaf and delirious, and was passing everything under her, two to four loose stools a day. On July 20th the blood was examined again, and it now exhibited well-marked leukopenia, only 2400 whites. On July 24th another solitary rose spot was observed. The recurrence of severe symptoms and of continuous high temperature, after the well-marked improvement that had taken place in the fourth week of the disease, clearly indicated that we had to do with a relapse. We gave her carbonate of ammonia 5 gr., syrup of tolu, and tincture of cinchona 30 ♏ of each, out of chloroform water, every four hours; and inhalations of oxygen. Carbonate of ammonia and bark is an old and very good prescription, recommended by Dr. Murchison for the typhoid state. Besides, it seemed well adapted for the bronchitis. This high temperature was maintained for a week, and then the general level of it became lower, viz. 103° F., and in ten to twelve days from the beginning of the relapse the morning intermissions again began to appear, and there were signs of a general improvement. At last, in the third week of the relapse—August 1st to 7th—the temperature became normal in the morning, and in the evening gradually fell from 102° F. to normal. Then there came a period of convalescence, which we were thoroughly glad to see, for she had been now five and a half weeks in the hospital and six weeks in bed, with fever all the time. There followed a week in which the temperature was normal and the general condition improved, and the bronchitis, which had been very refractory to treatment, cleared up of itself. But on August 15th the temperature again began to rise, and it rose in a way which is said to be almost characteristic of typhoid. Starting on the morning of August 14th at 100° F., it rose that evening to 102° F. On the 15th the morning temperature was 101° F., the evening temperature 103° F. On the 16th, in the morning, the temperature was 102° F., the evening temperature 104° F. This is the "step-like" ascent of temperature, which occurs in the beginning of enteric fever, but which you do not often see, because patients are rarely admitted to the hospital in the earliest stage of the disease. But in this relapse we could watch it well. For it was clear now that this girl had a second relapse. She maintained a high temperature from August 14th to 27th, and then she had a remitting temperature, going down in the morning, and up again in the evening, and finally, in the fourth week of the relapse, the temperature became quite normal again. During this relapse the bronchitis reappeared and was again severe. At the end of the second week the respiration rose up to 56 per minute. At the end of the third week (and in the twelfth week of the disease), the bronchitis improved, the temperature was normal, except for

an occasional rise up to 100° F., and in the succeeding week everything went on very well indeed. And now the patient got better and stronger in every way, and nothing further happened, except that she was constipated and her hair came out. On September 19th another rise of temperature began. This time it reached, on the 20th, 101·5° F., and it continued with intermissions to reach 100·5° F., until September 25th. On September 25th the maximum was 100° F., and on the 27th it was normal. Since September 27th there has been no more fever. She had already had, as I have told you, two relapses, one an intercurrent relapse, and the other a regular relapse. What this third rise of temperature meant was uncertain; Dr. Morley Fletcher, who then had charge of the case, considered it not to be a true relapse, because the temperature did not rise in a regular way, there were no new spots, and no recurrence of the bronchitis which had characterised the previous attacks. He thinks the rise of temperature was due to constipation. And certainly it did not last so long as the other two (only about a week), and it was not so severe, and since she recovered from it there has been no further fever.

Perhaps the most interesting points about this case are, first the bronchitis, and secondly the relapses. Bronchitis in a mild degree is very frequent as an accompaniment of typhoid, especially at the onset. But I think it is rare to get it so severe as it was in this case. At one time it seemed to endanger the patient's life. I notice that Osler, in his very excellent article about typhoid fever, says that "Bronchitis is one of the most frequent initial symptoms, indicated by the presence of sibilant râles. The smaller tubes may be involved, producing urgent coughing, and even slight cyanosis." This patient was more than slightly cyanosed; she was very blue and her breathing extremely bad. It occurred to me at first that we might possibly have to do with a patient who was the subject of chronic bronchitis, and that the typhoid had simply sufficed to light up an old disease. But it was not so, for the bronchitis completely disappeared in the intervals of convalescence, and reappeared regularly during the relapses; so it seems certain that it was a genuine part of the disease. Probably you will ask me was it a true infection of the bronchi, and were there typhoid bacilli in the sputum? That question I cannot answer because there was no sputum to examine, in spite of the severity of the bronchitis. The patient's state might be compared to that of a child who expectorates nothing; she was so ill that she did not pay attention to her cough and to getting rid of the sputum, but swallowed it. Dreschfeld, in his article in Allbutt's and Rolleston's 'System of Medicine,' says that the bronchitis of enteric fever is characterised by a short cough, *with little or no expectoration*. That was the case here.

The other point of interest seems to me to be the relapses. There were in this case two true relapses; first an intercurrent, or, as it is sometimes called, a subintrant relapse, coming on at the end of the fourth week of the disease, that is to say, after characteristic intermissions of temperature had begun, but before the temperature had become fully normal. And in that relapse she became as bad or worse than in the primary attack. In ten or twelve days more remissions again began and the temperature became normal in the third week of the relapse. After a week of normal temperature (and in the middle of the eighth week of the disease) she had a second relapse, the temperature rose in the characteristic step-like way and continued high for two weeks, and then there followed one week of intermittent temperature, three weeks' fever in all. And she had severe bronchitis, but her general symptoms were not as severe as before. Then after three weeks' normal temperature a third period came in which the temperature again rose. But it was not so high, there was no bronchitis, and no severe symptoms of any description. And so the question arose whether this third rise of temperature was due to a relapse or a complication, or what Osler terms a "post-typhoid pyrexia." The characters of a true relapse seem to be these: a step-like ascent of temperature, recurrence of the rose spots, recurrence of enlargement of spleen, and recurrence of any of the characteristic symptoms which you find in the original attack. The only difficulty about these things is that they may not always have been present in the original attack. In our patient, for instance, there were very few rose spots indeed and the spleen was never enlarged. As regards Widal's reaction, that test would not be of any use in the diagnosis of a relapse, because it would persist after the primary

disease. Complications, again, may raise the temperature; perhaps the most frequent of these are complications dependent upon some infection, such as boils or abscesses or necrosis of bone, or periostitis, or arthritis, or thrombosis of veins. Of course to identify them you would look for their local manifestations. And, as Osler points out, and I think it is a very good point, you will probably find in complications that there will be a rise in the number of leucocytes.

There remains the "post-typhoid variation of temperature," where the temperature goes up (or down) apparently for no sufficient reason. You must remember that the temperature of convalescents, and especially of the convalescents from typhoid, is a very sensitive thing; a very slight cause seems sufficient to raise it. Amongst the causes which are assigned for such elevation are constipation—which was what Dr. Fletcher supposed to be the cause in this girl's case—errors of diet, or excitement. The temperature may go up suddenly to 102° or 103° F., without constitutional or abdominal symptoms, and may remain high for two or three days.

As regards true relapses, the frequency of their occurrence varies, apparently in different epidemics and in different patients, and the percentages of relapses given by different authors are very different. Some authors say that 3 per cent. of the cases relapse, while others put the figure as high as 18 per cent. There are two kinds of relapse, both of which are illustrated in our patient: the ordinary relapse which sets in after the temperature has become completely normal, and the intercurrent relapse which begins before the primary fever has subsided. As to the number of relapses which a particular patient may experience, that also seems to be uncertain. It is not very infrequent for patients to have more than one. Osler quotes a case which is said to have had six distinct relapses, the whole course of the disease extending over eleven months four days. That must surely be a record. Ordinary relapses are said to be less severe and to last a shorter time than the original attack of the disease, and the mortality from the relapses is not so high. Still, I certainly remember examining post-mortem a case of Sir William Church's in which a patient died, in a relapse, of perforation. But concerning intercurrent relapses, Osler tells us that they are often most severe and that they are responsible for most instances of protracted typhoid fever. So that when a case of typhoid runs on for six or seven weeks it is probable that there is not one but two attacks, the second one catching up the first, and the two together merging into one long spell of fever.

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THE ÆTIOLOGY OF GOUT, RHEUMATISM AND RHEUMATOID ARTHRITIS.*

By C. WYNN WIRGMAN, M.D.Lond., F.R.C.S.Eng.

HEREDITY in disease is year by year growing more and more discredited. Its decline has coincided with, and is consequent upon, the rise of bacteriology. Once a visible cause can be assigned to a disease, fanciful speculation is at a discount.

With the discovery of the *rôle* of the tubercle bacillus, heredity's chief stronghold was destroyed. If one disease more than another seemed to be genuinely hereditary it was tubercle. Now the only shadow of that tradition is the decreased resisting power to the bacillus which is believed to be transmissible in certain individuals.

In cancer, the last Cancer Research Reports have shown that any hereditary tendency is extremely doubtful.

Its last remaining footholds appear to be in the disorders of the nervous system, and in that group of so-called constitutional diseases, such as gout, rheumatism and diabetes.

It is my object to discuss whether such a factor need be invoked in the gouty and rheumatic cases that come under our observation, or whether there is any constant pathological factor present which may lead us to a probable hypothesis of their origin.

Rheumatism and rheumatoid arthritis shade off into each other in such a way that it is impossible to say where one ends and the other begins. An acute attack of rheumatic fever may give rise to a chronic arthritic trouble which is identical with a typical rheumatoid arthritis. For all practical purposes they may be considered as different manifestations of one disease.

By the majority of observers to-day they are believed to commence from a microbic infection. Certainly the joint and cardiac changes cannot be clinically distinguished in their onset and course from forms that we see in other cases where the infective agent is known, as, for instance, in typhoid, where joint changes following an attack may mimic

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rheumatoid arthritis very closely, and again in gonorrhœal rheumatism, which is frequently mistaken for the subacute form of ordinary rheumatism.

Assuming, then, that rheumatism and rheumatoid arthritis are closely allied, why associate them with gout?

For the following reasons:

First, that between these two diseases and gout the only important differences appear to be that in the latter there is little tendency for the heart to become involved, and that in gouty subjects there is a deposit of some chemical combination of uric acid in various situations.

Secondly, with these exceptions gout appears to have no sharply defined borders whereby to differentiate it from rheumatism.

Thirdly, between the acute gouty and rheumatic local inflammations the only difference, apart from the deposition of urates, appears to be that in the former the skin is markedly reddened and that the sequelæ are not so important or permanent.

On the whole a microbic hypothesis of the origin of gout also seems by far the most probable. Why an inflammation which has all the characters of a microbic invasion should be attributed to a chemical cause has always appeared a mystery to me. Certainly all the forms of "irregular gout" (so-called) are such that, in the absence of this fetish word, they would unhesitatingly be classed either as toxæmias or as local infections.

It is a remarkable fact that though for centuries gout has had a classical symptom complex, never has an adequate ætiology been suggested.

Up to a few years ago heredity and errors of diet were the sole suggestions as to its possible origin. Recently much work has been done upon gout from the point of view of chemical changes in the blood and tissues. These, while most interesting and important, only take us back a step on the road and do not profess to elucidate its *primâ causa*.

So much for the relations of these three types of disease. I shall assume that a bacterial infection is the most likely source of origin, and will adduce clinical facts which have led me to the conclusion that it is the genuine one, and that it frequently commences in the same locality in these several diseases.

On what lines must we endeavour to solve their ætiology? There are two methods open to us—one, clinical observation, the other, bacteriological research. It is clear that if the bacteriological factor were obvious, in all probability it would have been discovered by now.

I will not enter into the many reasons for the difficulty of its determination, but will point out that there are other undeniable infections in which the assumed parasitic origin is either still undemonstrated or has only been proved within the past few years.

For example, none of us have the slightest doubt that scarlet fever and whooping-cough are infectious. They present all the typical features of an infection from without and can be transmitted from one person to another. We can, in the case of scarlet fever, make sure of not so transmitting it by the employment of careful disinfection. Nothing, in the absence of actual isolation of the organism, can be clearer proof of its material existence.

Sanitary precautions cannot extinguish a hereditary tendency though they may circumscribe its possibilities.

Another disease which may almost be said to have existed under a double personality is syphilis. It was regarded both as a typical infection and as a hereditary disease, in so far as the succeeding generation was concerned. Only very recently has its organism been demonstrated.

Poynton's views as to the offending diplococcus in acute rheumatism have not received universal acceptance, but it appears certain that, if not this, some other specific organism will ultimately be found.

Whether or no the parasitic origin can be demonstrated therefore need not affect our search for a clinical cause. The remoter results of chronic infections are now beginning to be recognised, though their bacteriology is yet unsystematised. Who doubts that ills follow as a result of chronic appendicitis, although to trace their bacterial genealogy is quite unnecessary. Without undue presumption we may try to track our symptoms to their clinical source without raising a side-issue as to the guilty one of all the various flora and fauna of the body.

In searching for the possible ætiological factors we must bear in mind two points. First, that an acute attack of an infection may arise from either an acute or chronic source elsewhere; secondly, that a chronic disorder probably starts from a chronic infection.

Where, then, are the usual sites of chronic inflammation? There are three situations where they are commonly found.

The first is the aural cavity and mastoid cells. So far as we know general disease very rarely follows suppuration at this point, though of course a septicæmia may spread in the ordinary way from an extension of the local disease.

The second is the naso-pharynx. Here we have two common sites of infection: (1) inflammation of the accessory sinuses of the nose resulting either from acute specifics or frequently, in the case of the maxillary antrum, from infection *viâ* the roots of the upper molars and premolars; (2) adenoids and infected tonsils.

The third is the alimentary tract, in which we include the buccal cavity.

As regards the intestines, we must first see whether they are the primary or secondary sites of infection.

It appears to me that intestinal affections which arise primarily in the intestines from errors of diet have no reason to be suspected in the production of rheumatism or gout. But when once there is a nidus of infection, diet may hypothetically influence it in many ways.

The next question is, From what points may intestinal sepsis be initiated?

Undoubtedly in adults buccal sepsis is the most common source, and in children adenoids and hypertrophied tonsils. In both of these there is a constant swallowing of pus or infective muco-pus, as a sequel of which digestive disturbances and inflammations are extremely common.

If we allow that these diseases are infective in origin it would appear that an auto-intoxication *viâ* the intestines is a very likely ætiological factor. Is there, then, any constant form of acute or chronic sepsis to be found in cases of gout, rheumatism, and rheumatoid arthritis? I have made it a routine practice to look for such in all these cases and so far have never yet failed to find one. In children, hypertrophied tonsils and adenoids, in adults buccal, or more rarely nasal and tonsillar disease, appear invariably to be present.

In children infected tonsils and adenoids are now believed to be almost always the cause of rheumatism. In adults pyorrhœa alveolaris is, I believe, the usual starting-point of infection.

There are a few cases on record in which antral suppuration appears to have been the *fons et origo mali*, but as this is so often due to dental trouble it may be classified under the same heading.

Acute tonsillitis in adults has always been recognised as a possible precursor of acute rheumatism; unfortunately, however, as it is by no means invariably present its importance has perhaps not been sufficiently recognised. To pyorrhœa, therefore, we may devote most of our attention as a less known site of possible infection.

We find, indeed, that careful attention to oral cleanliness is in many cases of the utmost value in treatment. Tomes has pointed out that antiseptic measures directed to the mouth can reduce the bacilli found in the large bowel 80 per cent.

The inference that because we have found a focus of disease and can cure it we can therefore cure its sequelæ is untenable. For one thing it is extremely doubtful if any general infection can ever be completely removed, and to argue that because general symptoms do not vanish after cure of pyorrhœa, therefore it was not the cause, is unwarrantable. It is certain that a large percentage of cases can be, if not cured, at least ameliorated by treatment of the gums, and if this is so it is unreasonable to abandon this hypothesis because a minority are not benefited.

Pyorrhœa alveolaris has derived its name from one of the most usual forms in which it is encountered, but the term must also be taken to include those chronic forms which exhibit a slow, dry, destructive osteitis on the one hand, and those rarer cases of fulminating alveolar infection on the other.

The first, *i.e.* dry osteitis, frequently passes into the typical purulent type. Less commonly the purulent ends in the dry.

The various forms met with probably depend on the patient's idiosyncrasies and on varieties in the virulence of the infecting organisms.

How or why pyorrhœa commences is not a subject on which I shall venture in this paper. Its importance has not yet received anything like the attention which it deserves. It is much to be regretted that the dental profession as a whole pay very little attention to the gums. Their sole concern appears to be with the teeth themselves and with mechanical appliances to take their place or supply their deficiencies. These appliances, I have found, frequently give rise to many of the more

serious types of pyorrhœa. Pus may be pouring from the gums, but it is thought very little of, and its danger and importance minimised. There are a few honourable exceptions to this, but it is the rule to find that although the presence of pyorrhœa may be pointed out by the doctor the average dentist actually denies its presence, or if he acknowledges its existence, undertakes to cure it in a short time. If he says so it means that he is ignorant of the disease. Naturally it is not easy for the medical man to be an expert in the early diagnosis of this condition, but if it occurs in such degree as to be a possible factor in disease, signs are usually to be found which should give rise to strong suspicion. A dentist with special knowledge should invariably be consulted, and if he is of opinion that the trouble is absent, our field of inquiry is, at least, narrowed.

I fully realise that until the bacteriology has been thoroughly worked out and placed on a sound basis my views as to its *rôle* in the causation of these diseases can only be in the nature of an hypothesis. Of course, the main difficulty in the estimation of its actual importance is the fact that pyorrhœa, in the poorer classes, is almost universal. So also is rheumatism. It is remarkable, however, that those whose mouths are really carefully kept are very free from these various ailments.

The symptoms and signs upon which a provisional diagnosis may be based are as follows:

Symptoms.—(1) Recession of the gums. This is *never* due to gout, but *always* believed to be so by the patient. Pyorrhœa may be diagnosed by this symptom alone. (2) Bleeding on gentle pressure caused either by mastication or tooth brushing. This is especially marked where the gums are swollen. (3) Soreness of the mouth and an objectionable taste. Tenderness of the teeth when eating sweets or masticating. This latter may be due either to exposure of the neck of the tooth or to inflammation of the maxilla. (4) Elevation of temperature for which no other cause can be assigned. This may reach 102° and 103° F.

The *signs* are as follows: (1) Abnormal colour. In the slighter stages the gums have the appearance of having been lightly brushed with strong carbolic acid. In other stages they are of a livid crimson, and in the most pronounced the colour is a bluish-purple. Redness of the gum where it encircles the teeth may be particularly noticed at the inner aspect of the upper molars. The normal colour of the healthy gum is pale coral or blotting-paper-pink. (2) Pus exuding from the socket. This can be shown in most cases by pressure of the finger from the base of the socket towards the edge. (3) The passage of a thin probe—a platinum wire is useful—for at least some eighth of an inch between the tooth and the gum. (4) There is a peculiar smell like mildewed hay which is almost always present unless masked by the smell of decomposition. It cannot be insisted upon too strongly that the *teeth* themselves are often quite sound; deficiencies or caries are only incidental accompaniments. The true seat of the disease is in the bone and soft tissues.

It must not be thought that symptomatic treatment of the various ailments mentioned above is cast on one side. All that is asked for in this paper is the careful examination of the case for septic foci and their removal when found. To suggest that acute rheumatism could be adequately treated by purely dental means is, of course, absurd.

It must never be forgotten, however, that when once any general infection is established, treatment of the primary focus or exciting cause cannot be expected to reach the toxins or bacilli circulating in the general system. This can best be explained by the analogy of syphilis where destruction of the primary site of inoculation, except in the very earliest stage, does not prevent systemic infection. But the repetition of the infection in the case of pyorrhœa gives the tissues no chance of renewing their resistance to the toxins against which we have no true specific as compared with mercury, so that local treatment in pyorrhœa is far more important than in syphilis.

At present we can arrange the various conditions met with as follows:

Pyorrhœa	with rheumatism, etc.
,,	,, gout.
,,	,, indigestion.
,,	,, various minor ailments.
,,	,, nothing pathological.
No pyorrhœa but a septic focus elsewhere	,, any of the above conditions.

It is only by careful tabulation of cases under some such scheme that data can be collected upon which to establish a theory.

Because a man has pyorrhœa it by no means follows that he must needs have any of the above diseases, for—

(*a*) He may be immune, either from inborn resisting power or self-immunisation.

(*b*) The organism may be of weak virulence and only locally harmful.

It will be understood then that the manner of infection may be either of a sapræmic or septicæmic nature. The first is more usually shown in the form of indigestion. The latter appears typically in the severer forms of acute rheumatism.

The following cases have been taken from my notes without any exclusion of those that do not fall into line:

	Symptoms.	Septic focus.
Gout:		
E. C. F—	Acute gout	Slight pyorrhœa.
L—	,,	Bad ,,
J. P—	,,	Bad ,,
C. W—	Gouty arthritis	Bad ,,
Rheumatism, etc.:		
A. B—	Rheumatism	Septic tonsils.
D. G. B—	Rheumatic arthritis	Bad pyorrhœa.
W. M—	Rheumatism	,,
F. C. B—	Rheumatoid arthritis	,,
A. H. R—	,, ,,	,,
W. Y—	Stiff neck	,,
R. W—	Sciatica	,,
J. W—	Rheumatism	Tonsils and adenoids.
H. N. L—	Rheumatic arthritis	Pyorrhœa.
H. J. K—	,, ,,	Very bad pyorrhœa.
N. J. B—	Lumbago	Pyorrhœa.
C. W. W—	Rheumatism	,,
Tonsillitis:		
D. H—	—	,,
H. L—	—	,,
L—	—	Very bad pyorrhœa.

I may say again that I have *never* failed to find pyorrhœa in an adult who has had rheumatism or gout.

As regards treatment of this somewhat intractable condition, *i. e.* pyorrhœa, it would seem that vaccine therapy is indicated. Unfortunately, as the bacilli are so numerous and their toxins not well understood, the only method in multiple infections at present is to make a serum from each case. So far the results, while most encouraging in simple infections, have not extended over a sufficient length of time for us to judge of their ultimate value.

The local treatment does not come within my province. I have to express my thanks to Mes J. G. and H. Watson Turner for the interest th have shown in the cases I have sent to them, a for their careful and skilful treatment.

I may say that it was a remark of Mr. J. Turner that originally turned my thoughts in t direction, and led to my investigating the conditi of the mouth as a routine practice.

Mr. JOSEPH TURNER said: Mr. Wirgman rai the question of the differential diagnosis of go rheumatism, arthritis deformans, including, I ta it, chronic rheumatism and muscular rheumatis I must confess that, as a dentist, I have be concerned rather to look for a possible underlyi common dental cause than to attempt to class the cases which have come under my observatic To illustrate the difficulty of classifying, *i. e.* diagnosing according to prevalent terms, let i quote from Professor Osler on "Gout." He say "After an attack or two in one toe, other joi may be affected, and it is just in such cases of po arthritis that the difficulty in diagnosis is apt to ari We have had of late years several cases admitted the third or fourth time with involvement of thr or more of the larger joints. The presence tophi has settled the nature of a trouble which the previous attacks had been regarded as rhe matic. . . . While pyrexia may be present, a often is, in gout, its absence is, I think, a valuat diagnostic sign. Many cases go a-begging for diagnosis. A careful study of the patient's hab as to beer drinking, of the location of the init arthritic attacks, and the examination for tophi the ears will prevent many cases being mistak for rheumatism or arthritis deformans." On t diagnosis of arthritis deformans he says: "T early stages may be difficult to diagnose fro acute rheumatism. The involvement of the small joints and the persistence of the condition in joint when once attacked are important poin In an advanced stage it can rarely be mistaken f either rheumatism or gout. Late cases are diffic or impossible to distinguish from chronic rhe matism."

We may take it, practically, that these diseas merge insensibly into one another. That grante it becomes obvious that it is possible that in large number of cases there is a common analogous underlying cause.

Naturally, nowadays, we turn at once to bacteria and suspect either toxic or actual bacterial infection.

Let me again refer you to Professor Osler (*cf.* "Rheumatic Fever," *ibid.*, p. 220): "Physicians have long been impressed with the striking similarity of the symptoms to those of septic infection." In the character of the fever, the mode of involvement of the joints, the tendency to relapse, the sweats, the anæmia, the leucocytosis, and above all, the liability to endocarditis and involvement of the serous membranes, the disease resembles pyæmia very closely, and may, indeed, be taken as the very type of an acute infection." Osler considers that it (rheumatic fever) is due to various pyogenic cocci, mainly streptococci, which cause a mild form of pyæmia; or to a specific streptococcus or diplococcus, but against this he points out the importance of salicylates on ordinary streptococcic infections, and that rheumatic joints never suppurate. Concerning arthritis deformans as a chronic infection he says: "The infection may be with a specific organism or perhaps with various ones . . . The influence of various infections such as gonorrhœa, influenza, etc., is important. . . . The acute onset with fever, polyarthritis, the presence of enlarged glands, and the frequent enlargement of the spleen, are all suggestive of an infection."

Of a possible infective origin of chronic rheumatism or of muscular rheumatism Professor Osler makes no note, but he allows that chronic rheumatism may follow acute or subacute rheumatism, though more commonly coming on insidiously in persons who have passed the middle period of life, and that persons of a gouty or rheumatic habit are more prone to muscular rheumatism.

No suggestion is made as to a possible infective cause of gout, though under irregular gout he says that attacks of what is termed "biliousness," in which the tongue is furred, the breath foul, the bowels constipated, the action of the liver torpid, are not uncommon in gouty persons—a very fair picture of the onset of an infective fever—but in view of the difficulties of diagnosis just enunciated and the strong suspicion of infection attaching to all the other members of the group, we may reasonably suspect such a cause, whether as a primary infection or as causing a preliminary upset of the intestinal tract.

In searching the body for a possible common source of infection the mouth cannot but arrest attention. In almost every human being it is germ-ridden, and it is capable of infecting the body either locally or *viâ* the intestinal tract, in which latter way it may initiate a chain of disturbed metabolism, apart from actual infection, which may conceivably end in gout. Among the germs found commonly in so-called healthy mouths are *Streptococcus longus* and *brevis*, *Staphylococcus aureus* and *albus*, *Diplococcus pneumoniæ*, besides such germs as *B. buccalis maximus*, whose pathogenicity is not determined, and I may remind you joint tissues are specially liable to staphylococcic infection; among occasional inhabitants *B. influenzæ*, *B. diphtheriæ*. True, many people hold that there are many useful germs normally inhabiting the mouth, though these yet remain to be deciphered, and that the continual presence of pathogenic germs tends to raise the body resistance. Unfortunately clinical experience does not seem to uphold this latter view. Of fifty-one persons lately examined thirty-eight had well-marked pyorrhœa alveolaris, *i. e.* resistance, so far from being heightened, was actually breaking down.

Perhaps my figure of infection seems high; in answer to that I must point out that the symptoms of pyorrhœa are very commonly overlooked. Pyorrhœa is a local disease due to stagnation—stagnation of germs and food *débris* among and around the teeth. In many people the gums along the fronts of the teeth where the brush easiest reaches are healthy, but inspection on the inner sides and between the teeth discovers the gums inflamed and well-formed pockets between the roots containing pus and decomposing food. Many mouths are pronounced healthy for want of minute inspection. The absence of swollen, bleeding gums and pockets exuding pus well within view of the first glance does not by any means exclude pyorrhœa. Every tooth must be examined in its whole circumference and every interdental space carefully probed (with fine dental probes) to make sure of the absence of pockets and of decomposing detritus between the teeth.

Turning again to the mouth as a source of infection, tooth-plates are commonly covered by a layer of germs; fillings whose edges overlap the tooth tissue of what is called the cervical edge, *i. e.* the

edge of the cavity nearest the gum; gold caps, crowns, and bridges presenting similar overlapping joints at their points of fixation or having parts inaccessible to cleansing all harbour myriads of germs, possibly good, bad, and indifferent—chiefly bad and so-called indifferent.

Now we have put forward a theory that these diseases—gout, rheumatism, arthritis deformans, chronic rheumatism, muscular rheumatism—may in many cases arise from a common or analogous source of infection, and that this source may be the mouth. Does it hold water? Most certainly it does. I have myself seen some of Mr. Wirgman's cases and have treated the mouth condition, and can bear witness both that the mouth was an efficient source of infection, and that the patient's condition improved. In these cases, however, the patient had the advantage of medical care; in the following case dental treatment stood alone with the exception of efforts to "sterilise the intestine." A man, æt. 50 years, had been treated for some years for gout. He had recurrent attacks of one big-toe joint, and at the time I saw him this joint was in a condition of subacute inflammation. He also suffered from recurrent attacks of irregular intestinal gout, as described by Osler. He was the subject of discharging pyorrhœa alveolaris of many years' standing. After some days' assiduous cleansing all his teeth were by degrees extracted, and his symptoms cleared up, including the big-toe arthritis. About eighteen months later he complained of a return of the intestinal symptoms. Finding his mouth and plates clean, I sought an analogous source of infection and found it in his nose. He was treated for early atrophic rhinitis by a nose and throat specialist, and again his symptoms cleared up. At present he remains better in health than he has been for years. This patient has arterio-sclerosis, and I suggest chronic toxæmia originating in the mouth as a possible cause of this condition. There would at least be nothing more strange in its production in this way than in its production by syphilitic toxæmia.

Now if you ask what is the treatment of this condition I answer "drainage." Cleanse and drain. Every pocket must be thoroughly cleansed and rendered drainable. This may mean laying open the pocket over a single rooted tooth; it may mean extraction of inaccessible teeth, or of teeth too loose, tender, and foul for treatment; it may mean alternate extraction with a view to isolation of the remaining teeth.

On account of the difficulty of access the infected pockets are specially difficult of treatment. The number of remedies recommended shows their ill-success; in fact, the success of local remedies depends on the manner of use.

Whatever antiseptic is used must be used weak enough not to injure the tissues, and must be introduced well to the bottoms of the pockets with the idea of mechanical cleansing as well as of inhibiting bacterial growth.

As a general rule the cleansing should be repeated at first on three alternate days, and later at longer intervals according to the clinical progress of the case, the hope being that at each succeeding visit there will be fewer and less virulent germs to be dealt with, till eventually intervals of two or three months may be permitted.

Owing to the difficulties of drainage and the chances of re-infection absolute cure is almost hopeless.

Tartar must be removed as far as possible. Myself, I use citric acid dissolved in hot acid carbol 1–40, which I find combines the cleansing action of citric acid with the bactericidal or inhibitive action of carbolic acid; and at the same time I teach the patient to rub his gums with a clean rag dipped in a dilute antiseptic, with the idea of emptying all accessible pockets, and to use waxed silk to remove *débris* from between the teeth and to scour their interstitial surfaces, as well as enforcing the usual brushing.

Of the use of vaccine therapy in pyorrhœa it seems to me too early to speak. Certainly general symptoms clear up wonderfully under vaccines prepared from mouth organisms, but the difficulty of drainage greatly discounts their value in the cure of the local condition. Perhaps some cases of gouty eczema might respond to such treatment.

It seems to me that by approaching this group of diseases—gout, rheumatism, arthritis deformans, chronic rheumatism, muscular rheumatism—from the bacterial standpoint, without worrying ourselves over nomenclature, we shall be able to split off a large block as being truly infective, the source of infection being often no more recondite than the mouth. Later we may be able to give them names more expressive of some salient feature of the disease than "irregular gout" or "chronic rheumatism."

May 24th, 1909.

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WITH MR. BLAND-SUTTON AT MIDDLESEX HOSPITAL.

VIII.

ON CANCER OF THE GALL-BLADDER AND BILE-DUCTS.

IN the last lecture I reiterated, with perhaps depressing monotony, that primary cancer of the gall-bladder is an insidious disease rarely accompanied with definite signs and symptoms until the disease has passed beyond the bounds of hopeful surgery. In describing cancer of the large extra-hepatic ducts, including the ampulla, I shall have to repeat that when this disease arises in these ducts it begins insidiously and gives rise to few signs, but it differs from cancer of the gall-bladder in one important particular, namely, jaundice; this is the earliest and most persistent sign when cancer attacks the ducts forming the excretory apparatus of the liver. One of the features which will probably attract your attention when you have an opportunity of studying a recent case is the small amount of cancerous material which leads to such disastrous consequences. Fortunately, a primary cancer in any portion of the extra-hepatic ducts is rare, but a sufficient number of cases have been recorded to allow a systematic account of the chief clinical features of the disease to be written.

Cancer may arise at the junction of the two hepatic ducts, or at the union of the hepatic and cystic duct, or in any part of the common duct, or in the ampulla itself. Carcinoma arising in the head of the pancreas and in the mucous membrane of the duodenum, near the bile-papilla, will obstruct the outflow of bile and produce symptoms indistinguishable from those due to cancer arising in the common duct, and of these obstructive jaundice is the most obvious. To the naked eye cancer of the bile-ducts looks like a knob of tough fibrous tissue blocking up the duct; in some cases

the duct appears as if embedded in a mass of tough fibrous material, but on microscopic examination this growth is seen to be made up of columnar or spheroidal epithelium, and in some specimens a tubular or gland-like arrangement is obvious, in which case it is sometimes termed an "adeno-carcinoma." In all cases, however, the blockading effects on the ducts are the same, although the precise results produced vary according to the position of the obstruction. These varying effects are carefully studied by surgeons, as they are useful aids in what is known as differential diagnosis. For example, the presence of cancer in the extra-hepatic ducts not only completely hinders the escape of bile into the duodenum but leads to dilatation of the canals above the obstruction, including the intra-hepatic canals. This also induces, as a consequence, enlargement of the liver, and, in some cases, the intra-hepatic canals are so dilated that a section of the liver resembles a sacculated kidney (Fig. 1).

The situation of cancer of the bile-ducts is important in its effects upon the gall-bladder, for when the disease arises at the junction of the two hepatic ducts—a common situation—the supply of bile to this receptacle will be cut off, whereas when the blockade is well below the junction of the cystic and the hepatic duct the gall-bladder will become over-distended with bile, and can often be felt as an oval body lying in the hypochondriac or right lumbar region. It may be mentioned here that the condition of the gall-bladder is a valuable guide in the differential diagnosis of obstructive jaundice. It has been determined by observation that when escape of bile into the duodenum is completely arrested by cancer in the common bile-duct, or the ampulla, or when cancer arising in the head of the pancreas implicates the common duct, the bile-ducts and the gall-bladder become distended and dilated in response to the pressure of the bile accumulated within them. In these circumstances the gall-bladder will become so big that it may be felt as a large, pear-shaped lump lying in the right lumbar region. When the cystic duct is obstructed the gall-bladder passively enlarges from the accumulation of the mucus secreted by its own glands. On the other hand, when the common duct is occupied by calculi the gall-bladder is smaller than usual, and is, as a rule, tightly contracted on any biliary concretions it may contain. For detecting these contrasted conditions we are indebted to Courvoisier. This rule is sufficiently constant to be useful in practice, but there are exceptions, and it may be useful to describe one.

For instance, it was pointed out in dealing with cancer of the gall-bladder that this disease may arise in the mucous membrane in any part of this

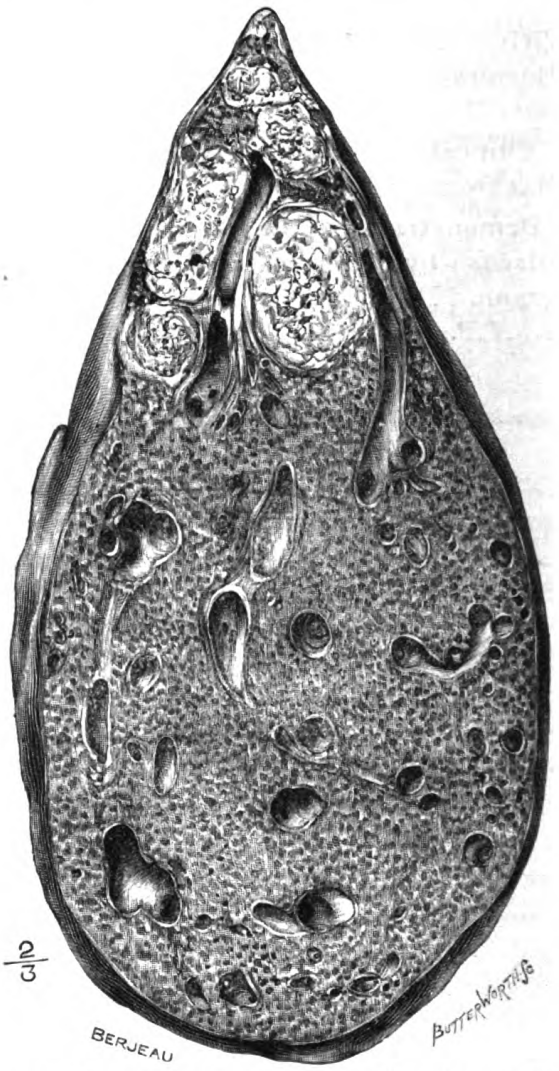

FIG. 1.—Liver in section, showing dilatation of the intra-hepatic bile-canals secondary to primary cancer of the common duct.

receptacle. Thus in the specimen represented in Fig. 2 the cancer arose in the neck of the gall-bladder and extended into the cystic duct, and formed a sort of collar around a solitary gall-stone. Even such an extensive mass of cancer in the neck of the gall-bladder would not cause jaundice. It is, however, easy to realise that if the cancer extended along the cystic into the hepatic duct there would

be obstruction to the escape of bile from the hepatic duct, which would lead to jaundice. Such a case has been observed and carefully recorded.

The great interest of these cases centres around the diagnosis. When a patient suffers from persistent, profound and unvarying jaundice, it at once becomes an important question for the patient's welfare to determine the nature of the obstruction. If the blockade is due to a gall-stone in the common duct, or in the case of persistent and profound jaundice accompanied by emaciation, to the

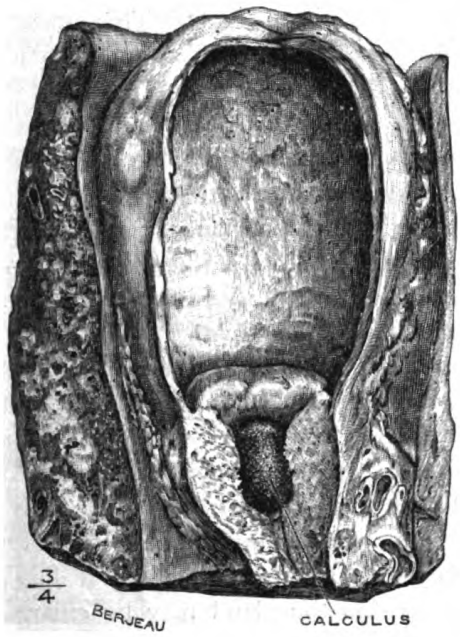

FIG. 2.—A gall-bladder with a primary cancer arising in its neck and extending into the cystic duct. The gall-bladder was filled with pus. The patient, a man, æt. 70 years, died nine months after the beginning of his symptoms. (Museum of Charing Cross Hospital.)

consequences of a calculus in the ampulla which not only blockades the bile-duct, but also the pancreatic duct, it is an important matter to remove the obstructing stone. An operation in these circumstances will in all probability prolong the patient's life. On the other hand, if the obstruction be due to cancer the patient will not be benefited and perhaps his life will be materially shortened.

Until you become more thoroughly acquainted with the difficulties of diagnosis, you will often be astonished to watch a surgeon open the abdomen of a patient deeply jaundiced hoping to find a calculus in the common duct, or in the ampulla, and on examining the duodenum with his fingers he finds a hard body occupying the position of the bile papilla, yet he cannot satisfy himself of its nature. He then makes an incision into the wall of the second portion of the duodenum and exposes the papilla, still hoping to find a stone in the ampulla, but to his chagrin finds a small knob of cancer. In such a case Halsted found a carcinoma of the ampulla which he promptly excised with the bile papilla and the adjacent section of the common duct; the cut end of the duct he implanted into the duodenum. The patient recovered from the operation, but died several months later from recurrence. Similar cases have been recorded. The operation of removing a gall-stone from the ampulla by means of an incision through the duodenum is known by the portentous term "trans-duodenal choledochotomy." It is an interesting and satisfactory procedure, and if you carefully watch the parts as the surgeon gently squeezes the stone through the opening after incising its edge, the escape of the calculus is followed by a jet of fluid. This is usually bile, but sometimes it is clear fluid; in the latter case this is of serious import, as I will endeavour to explain.

When the escape of bile into the duodenum is completely cut off the liver continues to excrete bile, and the pressure in the bile-ducts will continue to rise until resorption takes place and the bile finds its way into the blood, causing that yellowness of the tissues which we call jaundice. The bile under such pressure finds its way into the inter-lobular lymphatics, and is carried into the thoracic duct and thence enters the blood-stream. When this mingling of blood and bile (cholæmia) has existed for several weeks the coagulation-rate of the blood is lowered, and it is an established fact that operations on patients who have been deeply jaundiced for several weeks are liable to be complicated with an uncontrollable oozing of blood, and the patient bleeds to death in the same manner as after splenectomy performed for a leukæmic spleen. I learned this fact very early in my surgical career. I read books devoted to diseases of the liver for the purpose of ascertaining particularly in cases where the escape of bile is prevented by cancer of the duodenum invading the papilla ("circum-ampullary cancer" as it is sometimes called), or when it arises in the head of the pancreas, whether the lethal effects of the

cancer are in any way hastened by the consequent jaundice. No information was forthcoming. This induced me to try the effect of conducting the bile into the intestine by anastomosing the gall-bladder and the transverse colon.

My first observation was made on a woman jaundiced in consequence of carcinoma of the head of the pancreas. In this instance the skin was of that deep green hue which is sometimes called "malignant" or "black jaundice." The gall-bladder, which could easily be felt as a large ovoid body lying below the ribs, was exposed through an incision in the line of the right rectus muscle, and through a small opening made at its free end the bile was allowed to run away; the edges of the opening were then sutured to the edges of a hole made in the wall of the transverse colon immediately adjacent. The wound in the abdominal wall was carefully closed with sutures. During the two days following the operation an enormous quantity of bile escaped by the anus, indeed, the patient suffered for forty-eight hours from a profuse biliary diarrhœa. During this period the wound oozed blood freely, and nothing would check it. She died a few days after the operation, and we found that a similar oozing of blood had taken place around the edges of the wounds made in the colon and gall-bladder for anastomotic purposes, and in the tracks of the sutures; and no union had occurred between the gall-bladder and the colon. Since that date I have been successful in several cases in effecting a junction between the gall-bladder and colon in patients with obstructive jaundice due to cancer by performing the operation at an earlier stage, that is, before the jaundice became too intense. As a result of these operations I have satisfied myself that jaundice does not hasten the fatal event, except in so far as it directly imperils the patient's life from hæmorrhage when operative measures are undertaken. It is well, therefore, that you should be informed on this point, that in severe and progressive cases of jaundice where there is difficulty in deciding whether the obstruction depends on a calculus impacted in the ampulla or a cancer in that situation, the matter can only be determined in the course of an operation, therefore surgical interference should not be deferred until the jaundice is of such intensity that an operation is attended with grave risks from hæmorrhage, nor should you be induced to embark on such an undertaking in the belief that by giving the patient chloride of calcium you may be able to increase the coagulability of the blood. Let me also remark that if you explore the bile-ducts and find the escape of bile obstructed by cancer, either of the common duct, the ampulla, the duodenum, or the head of the pancreas, you will make your patient comfortable and certainly earn his gratitude by anastomosing the gall-bladder with the duodenum, or jejunum if you can, or with the colon, as this will relieve the jaundice and the intense itching (pruritus) of the skin which is such an intolerable nuisance to icteric patients. This operation is denoted by the sesquipedalian term, "cholecyst-enterostomy."

There are one or two facts connected with obstructive jaundice due to diseases of the head of the pancreas which are worth attention. When cancer arises in the head of this gland it causes jaundice by obstructing the terminal segment of the common bile-duct, which either traverses a canal in the gland or lies in direct contact with it. The actual obstruction may be due to pressure on the duct, or this structure is sometimes actually implicated by the malignant growth.

The method of determining whether the jaundice is due to cancer in the head of the pancreas in the course of an operation may be described as "rough and ready," for it consists in simply feeling it with the fingers. As the gland may be enlarged and hard from chronic pancreatitis as well as from cancer, the fingers are unable to distinguish between the two conditions. It has happened that in cases where cholecyst-enterostomy has been performed as a palliative measure under the impression that the patient's trouble was due to cancer, he has recovered, the tumefaction of the pancreas being really due to pancreatitis.

There is, however, a peculiar tint about the jaundice associated with cancer of the head of the pancreas which greatly assists diagnosis. The jaundice, which is usually unaccompanied by pain in the early stages of this disease, lacks the saffron yellowness which is seen when the common bile-duct alone is obstructed, and assumes a somewhat mahogany tint, which is very characteristic, and in those patients in whom the bile has been successfully diverted into the alimentary canal the yellow element in the colouration of the skin and the itch-

ing disappear, but the peculiar brown tint, which resembles the bronzing of Addison's disease, persists. No satisfactory explanation of the brown hue of the skin is forthcoming. It is, however, a valuable aid in diagnosis.

It has already been mentioned that when the flow of bile along the common duct is completely stopped by an obstruction of any kind, the bile is drained away by the lymphatics into the circulation and its final escape is effected by the kidneys. In the early days of the obstruction, if the common bile-duct be exposed and incised in the course of an operation it will be found distended with bile. When the blockade of the duct has been maintained many weeks (six or more) it happens now and then that the duct no longer contains bile, but a colourless fluid, probably mucus. This is a sinister sign, for surgeons who have had a wide experience of what is conveniently called "gall-stone surgery" state that in these circumstances the patients almost invariably die. My observations agree with this.

It should also be mentioned that in some cases of cancerous obstruction of the common duct the gall-bladder becomes so distended with bile, or bile mixed with pus, that the wall ulcerates, and then a perforation occurs and the patient dies from acute peritonitis due to the escape of septic material which it contained. Careful records of such disasters are available. I have known a case of primary cancer of the gall-bladder to terminate in this way.

Cancer in the excretory ducts, like this disease in the gall-bladder, is most common between the fiftieth and sixtieth years. It is also useful to bear in mind that cancer in any situation in the excretory apparatus of the liver is not usually accompanied by pain. It, however, must always be remembered that a gall-stone may painlessly obstruct the common duct producing profound jaundice; on the other hand, cancer will sometimes obstruct the duct and set up attacks of pain resembling biliary colic.

The great point in which cancer of the common bile-duct, or its ampulla, differs from cancer of the gall-bladder is this:

Cancer in the gall-bladder nearly always co-exists with gall-stones, whereas the presence of gall-stones in association with cancer of the common bile-duct is exceptional.

Cancer of the Duodenum in relation to Obstructive Jaundice.

Primary carcinoma in any part of the small intestine is uncommon, but it occurs more frequently in the duodenum, short as it is, than in the jejunum or ileum. It is also remarkable that the pylorus should be so frequently attacked by cancer—indeed, it is one of the three commonest situations in which this disease arises—while the succeeding twelve inches of the alimentary canal is almost immune, yet it is often the seat of ulceration. There can be little doubt that a cancerous ulcer of the duodenum would often escape detection were it not for the fact that the disease is apt to arise in the immediate vicinity of, and often involves, the bile papilla, leading to obstructive jaundice. This circum-ampullary carcinoma of the duodenum leads to distension of the bile-ducts and the gall-bladder, but the course of the disease differs somewhat from that seen in cases where the disease arises in the ampulla or in the common duct, because the cancerous ulcer on the surface of the duodenum is liable to become infected and then it sloughs; the infection will extend into the bile-ducts and set up suppurative cholangitis with its usual accompaniments, fever and rigors, ending in death from sepsis.

I may take this opportunity of relating the facts of a somewhat unusual case of cancer of the duodenum which has some bearing on the subject in hand. A man, æt. 56 years, was invalided from Burma on account of persistent vomiting and rapid emaciation. A malignant growth somewhere in the gastro-intestinal tract was suspected but no lump could be felt anywhere. The vomiting resembled that seen in the condition known as "vicious circle," which occasionally happens after the operative procedure known as gastro-jejunostomy. I decided to set the diagnosis at rest by examining the alimentary canal through an abdominal incision. The stomach, the small and the large intestines were examined carefully and nothing appeared to explain the symptoms, but on turning the stomach upwards to examine its posterior surface I saw a small contracting growth in the middle of the third part of the duodenum. This hard ring of growth had completely obstructed the lumen of the duodenum so that the bile and pancreatic juice regurgitated into the stomach,

where it mingled with the gastric juice and ingested fluids, to be ejected in the form of filthy vomit.

The duodenum above the stricture was enormously dilated and produced an appearance not unlike a double stomach. The growth had involved the duodenum and was so closely adherent to the superior mesenteric vein that its removal could not be entertained. I performed posterior gastro-jejunostomy and then anastomosed the greatly distended duodenum with the limb of the jejunum descending from the new stoma, so as to drain the bile and pancreatic fluids direct into the small intestine.

The immediate results of the operation were admirable. The vomiting ceased and the patient began to take and assimilate food; his pain ceased and we entertained hopes that his life might be prolonged. About thirteen days after the operation he had severe cardiac dyspnœa, then circulatory troubles supervened, from which he died. However, the last fourteen days of his life were made comfortable by the operation.

The Relationship of Gall-Stones to Cancer of the Gall-Bladder.

It has been already mentioned that the frequent association of gall-stones and cancer of the gall-bladder has led some surgeons to regard a calculous cholecystitis as a pre-cancerous condition. Let us review the facts and satisfy ourselves as to how far they support this view. Careful observations and investigations into the conditions underlying the formation of gall-stones, especially by Naunyn, have shed much valuable light on this matter. Gall-stones are mainly composed of cholesterin, and this material is collected around a nucleus which may consist of shed epithelium and clumps of bacilli; the cholesterin is mixed in varying proportions with a cementing substance known as bilirubin-calcium. Cholesterin was formerly regarded as a deposit from the bile, but it is now known that this singular stuff is furnished by the epithelium lining the gall-bladder and the larger ducts, especially when inflamed. Occasionally the crystals of cholesterin can be seen on the mucous membrane of an inflamed gall-bladder, sparkling like the tinsel on the coat of a harlequin. Many observations have been published in which an attack of typhoid fever preceded the cholelithiasis, and the *Bacillus typhosus* has been found in the gall-bladder twenty years or more after patients have recovered from the attack of typhoid. Moreover the relationship between micro-organisms, cholecystitis, and gall-stones has been established by the experimental production of gall-stones after injecting attenuated cultures of micro-organisms into the gall-bladders of dogs. It is now regarded as proved that the favouring conditions for the formation of gall-stones are catarrh of the epithelium lining the gall-bladder and the bile-ducts, and the presence of micro-organisms, especially *B. typhosus*.

A valuable demonstration of the origin of cholesterin from the epithelium of the gall-bladder is afforded by those cases in which the cystic duct is so completely plugged by a calculus that bile no longer finds its way into the gall-bladder. In these circumstances the gall-stones which form subsequent to the obstruction of the cystic duct consist of pure cholesterin and look like polygonal lumps of spermaceti. The same conditions exist in cases where the cystic duct is plugged by cancer.

One of the first conclusions which is forced on the mind of the surgeon when he reflects upon the condition of organs antecedent to the occurrence of cancer is that this dread disease is more liable to attack an organ which has been the seat of previous disease than one which is obviously healthy. The opinion which I hold very strongly is this: The pathological conditions of the epithelium lining the gall-bladder which cause it to produce cholesterin in abundance increase its vulnerability to the micro-parasite of carcinoma. It is illogical to urge that cancer of the gall-bladder is due to gall-stones when this disease occasionally arises in a gall-bladder which has never been occupied by calculi; moreover, when cancer arises in the large excretory ducts of the liver it is exceptional to find the disease associated with cancer.

The fact that patients with chronic calculous cholecystitis are more liable to carcinoma of the gall-bladder than an individual with a healthy bile-receptacle, is used, and rightly, as an argument that such calculi should be removed by operation. I go a step further and urge that such unhealthy gall-bladders should be removed. This recommendation has been questioned on the ground that there are very few instances known in which patients who have had biliary concretions removed from their gall-bladder (cholecystotomy) have again come

under observation with cancer of the gall-bladder. This side of the question has not been investigated with any zeal. I have satisfied myself by following up the after-history of patients who have had cholecystotomy performed and have passed out of the hands of the surgeon with a biliary fistula, that some of them have died from cancer of the gall-bladder. In one instance known to me the patient had a biliary fistula five years before cancer supervened. If more attention is given to this matter, and its importance be realised by those who have the care of patients with persistent biliary fistulæ, some valuable evidence would soon be available. The more I study this aspect of the "gall-stone question," the more convincing the evidence appears, that when an operation becomes necessary for calculous cholecystitis the surgeon acts in the best interests of his patient when he removes the diseased gall-bladder.

May 31st, 1909.

The Toxic Secondaries of Chronic Tonsillar Disease.—A. R. Elliott declares that many grave and fatal infections enter the body through the tonsils, such as endocarditis, rheumatism, scarlet fever, tuberculosis, etc., and in addition to these specific processes other less virulent and non-specific organisms may become established there and poison the body with their toxins. When the latter once gain access to the circulation they exert certain catalytic and hæmolytic effects, which, if the toxæmia is long continued, may eventuate in organic degenerative changes or abnormal blood states. The most common secondary from chronic tonsillitis is anæmia of the simple type. Many tonsils in these patients contain crypts plugged with all sorts of *débris*, which soon becomes cheesy and foul smelling. Another condition frequently associated with chronic tonsil disease is rheumatism. Absorption of septic toxins from the tonsils may so lower the vital resistance to infections that the individual becomes liable to certain minor infections, such as styes, furuncles, and acne. Also herpes and erythema have both been observed in connection with tonsil infections.—*Medical Record*, vol. lxxv, No. 20.

A CLINICAL LECTURE
ON
SYPHILIS.

Delivered at St. Bartholomew's Hospital.

By HARRISON CRIPPS, F.R.C.S.,
Surgeon to the Hospital.

GENTLEMEN,—I propose to-day to say a few words about syphilis. I am sorry I cannot oblige some anonymous gentleman who was good enough to write me a letter suggesting that I should give a clinical lecture on gonorrhœa. Syphilis is a very different disease now in this country compared with what it was some two hundred years ago. Of course we do not know really when syphilis was introduced into Europe. So far as I know, there is no record of syphilis before the end of the fourteenth and fifteenth centuries, and the supposition is that it was introduced into Europe from South America. Of course in the Old Testament there is an allusion or two to difficulties which a certain man got into—I forget who—for it is described that he had running sores in the groin and aching of the bones. And, of course, these running sores are much more likely to have been connected with a soft sore than with true syphilis. When one comes to read the description of the syphilis of one hundred or one hundred and fifty years ago, such as Hunter described, and also when we examine the specimens in the different museums of syphilis at a later date, one cannot but be struck with the fact that it was a very much more severe disease than we see nowadays. In other words, syphilis, especially in the north of Europe, appears to be to a great extent dying out as regards its virulence. There was a time when if a man had syphilis he ran the risk of losing a portion of his nose, the bones of his head, and practically becoming a cripple for the rest of his life. But nowadays we very rarely see cases of that description. The ordinary respectable West-end syphilis of to-day is generally quite a slight disorder, easily treated, and the patient is well in about six months, and seldom gets any signs of tertiary symptoms. That gradual dying out of a disease has not only been noticed in regard to syphilis, but in regard to many other varieties of disease. Take, for instance, measles.

That disease in this country is a mere nothing, with a very slight mortality; whereas, on the other hand, when we introduced measles into the South Sea Islands and Fiji about half a century ago, the inhabitants there had some very virulent attacks of measles, so severe that something like 20 to 30 per cent. of the cases attacked died. In other words, we planted a disease into a new soil, and it then became very virulent. In a similar way if you plant a virgin field with wheat you produce a fine crop, far better than if that field has been used for wheat for some years. So in that respect measles is a slight disease in this country, and syphilis seems to be acting in the same way. But if you put syphilis into a country which has not had it, it will be very virulent. If ever I see a really bad case of syphilis, I nearly always find that it has been caught from some of our colonies, especially from the South Sea Islands. Therefore when one is considering about the severity of syphilis with regard to it affecting an individual, I think there are two items which come into play. First of all there is the original disease. A man may get what is called a very mild inoculation, such as he would get in this country, and have the disease only slightly, or he may get a very virulent inoculation, such as a direct importation from a new country where it has not been in existence for long. There is another element in the severity of an attack of syphilis, and that is the personal element quite apart from the character of the disease. It is undoubted that if the patient has a broken constitution from any cause, say that he is tubercular or he is gouty, or, above all, if he is alcoholic, you find that that patient almost invariably has a far more severe attack of syphilis than if he had been a perfectly steady man. I often tell my class when I am talking about syphilis, as indicating the fact of the virulence of the poison from a new country, that perhaps the worst case of syphilis I have ever seen was the case of a commander who was in Her late Majesty's navy. He came to see me many years ago, and I remember all the circumstances of the case perfectly well. He was invalided out of the Service; he had iritis, so that he could not see properly out of one eye, he had lost a considerable portion of his nose, he had two or three large holes going nearly through his scalp, with necrosis, he had ankylosis of one shoulder, and, in fact, he was a regular cripple. He told me that the way he got the disease was that he landed with a boat's crew one night off Fiji, and I do not know exactly what happened, but a few weeks afterwards he noticed a sore on the penis, which became very large and troublesome, and was obviously a chancre. And from that time he dated his illness. I got to know him fairly well, and in conversation he said: "The curious thing is my first lieutenant was out with me that same evening in the same boat's crew. I do not know whether it was the same lady, but he got into difficulties; he is in London now and I have told him about you, and he is anxious to come to see you." I said, "Yes, by all means." In due course the lieutenant came down to see me. It is true he was not in such a bad predicament as his senior, but I think his was about the second worst case of syphilis I have seen. It was very virulent; there was necrosis of parts of the bones of the nose. Now those two cases of such virulence obviously occurred in healthy and temperate men, because they were in the Royal Navy. They had received their syphilis from a very virulent source, from the virgin soil.

The first thing to be done when you see a case of syphilis is to make a correct diagnosis as regards the sore itself. I will not go into all sorts of obscure things, like the epithelioma, etc., which a sore might be mistaken for. In practice there is only one thing which will give you much trouble in diagnosis. You say to yourself, Is this sore on the penis true syphilis, a hard sore, or is it merely a chancroid or soft sore which is not followed by syphilis at all? How shall you tell, when you see a patient and he has a sore on his penis, whether it is a true Hunterian sore or merely a chancroid? The history is of course very important if you can rely upon it. A soft sore shows itself within four or five days of being caught. A true Hunterian chancre very seldom shows itself before the twenty-first or twenty-second day after the disease has been caught, generally later. So if the patient says he had a connection five or six days ago, and that he noticed that trouble yesterday, and that he has had no chance of catching anything for some months previously, whatever that is it cannot be a true Hunterian chancre; it would not have shown itself in the time. But unfortunately you cannot rely on what patients tell you as to when they caught their sore. And it is very curious that any man thinks that any little trouble he has got into

of that kind such a short time as a week ago must be an immoral event, but with regard to anything which happened three weeks or a month ago, time has cleared his character, and that he has become a reformed person since. Hence patients often date the time of inoculation far longer back than the real time. You will have, perhaps, an elderly colonel coming to you, and he says he does not know what is the matter but he has an irritation on his penis, and he would like you to look at it. He produces it, and you see it looks like a soft sore. And you say to him: "When do you think you caught this"? "Catch it, sir? I have not caught anything; quite impossible; nothing of that kind." You talk to him a bit, and then you say again: "Just think and consider." He says, "Well," and you follow that up by saying, "It is very important you should let me know when you caught it." He will then perhaps say, "Yes, now you remind me, there was a chance five weeks or a month ago; I have just thought of it." I say: "Just bring your mind back to last Sunday." He says: "By-the-bye, Doctor, it slipped my memory; there was a chance of catching it." As a matter of fact, unless you cross-examine your patients very closely in that way it is very difficult to rely on the history they give you. If you can rely upon it, it is a very considerable help in arriving at a diagnosis.

Now with regard to the sore itself. There are certain characteristics of a hard sore, and certain characteristics of a soft sore. I will take the soft sore such as it would look if it had been in existence perhaps four or five days before you saw it, and when the patient sees you it is fairly well developed. You find that in that period the sore which is not going to turn into syphilis is a true ulceration, it is a destruction of epithelium, and sometimes it even destroys the true skin. So that you get an ulcer. The ulcer will be depressed. Now a hard sore is just the reverse of that. It is not a destruction of the true skin at an early stage, but it is an infiltration of the epidermis, so that the epidermis is raised, forming a sort of flattish lump. It is true that the surface of this is excoriated and raw, but that is because there is a desquamation of the epithelium; it is not at that stage a true ulcer, and generally speaking from first to last it never does really ulcerate. Sometimes, especially with patients who have a broken constitution, in two or three weeks there is a tendency for this infiltrated tissue to ulcerate. What is another characteristic of soft sore, as compared with true Hunterian sore? The true Hunterian sore is nearly always single; soft sores are generally multiple. So if there are two or three sores you may say it is not absolutely impossible it may be syphilis, but the chances are fifty to one that it is not. Then the appearance of the sore as regards its secretion. A soft sore is always covered with some purulent secretion, and a fair amount of it. A hard sore at an early stage has a glutinous, semi-transparent exudation, and often very little of this. Then with regard to the feel, and when you feel these sores do not put your naked finger on, but smear some vaseline over it first, for that will prevent inoculation, but even then I prefer a tiny layer of cotton-wool over it. The moment you feel a hard sore between the finger and thumb you are struck with the hardness of it, just as if there was a foreign body put under the epithelium. On the other hand in the case of a soft sore you hardly feel any induration at all. As its name implies, it feels soft. With regard to the condition of the glands in the groin, you often find one enlarged gland in each groin in a soft sore with a great tendency for it to suppurate; it is very tender and very large, and at the end of a week there is a tendency for it to break down and form a suppurating bubo. There are enlarged glands in syphilis, but there are generally two or three glands involved on each side, and although they reach a considerable size they are not very tender. It is very rare for the glands in true syphilis to suppurate.

Now, gentlemen, I have given you the outlines by which, in many of these cases, you will be able to distinguish between true syphilis and a chancroid lesion. If you consider those points, and if you have had a reasonable amount of experience in seeing cases of syphilis, you will find that in nine cases out of ten, when you hear the history and see the sore, you will be able to pronounce a fairly positive opinion. You will be able to say on the one hand, Do not bother yourself about this. On the other hand, you will tell the patient it is a serious matter, as the condition he has is syphilis. But whatever experience you may have had—you may have seen hundreds of cases, and when I had charge of the Skin Department of St. Bartholomew's Hospital I

saw hundreds of cases—there will be cases which you cannot diagnose for a certainty, as I have found myself. In about 10 per cent. or 12 per cent. of the cases I saw I could not express an opinion. There are certain characteristics of a hard sore which ought to have been there, but were not, and there were certain characters of a soft sore which were present and ought not to have been present if it was soft sore. As I say, in a certain number of cases you cannot make a diagnosis until time has solved the mystery. What course does the hard sore run? It is generally apparent about the thirtieth day after it has been caught. Then it gradually increases in size (at that time it is small), and in about a fortnight it has got to about its maximum, and its maximum size varies very much. In the ordinary London case it is about the size of the surface of a three-penny-piece, but I have seen the sore as large as half-a-crown. But during a fortnight it will reach the biggest size it is likely to arrive at. It will then remain stationary, neither diminishing nor increasing, for perhaps another fortnight. So that is a month after the patient first noticed it. And then, especially under treatment, it will gradually disappear, it will heal over at the margins, and at the end of another fortnight or three weeks it has practically gone, leaving only a little hardness in its site. So you can tell your patient that from the time he first noticed the sore till it has disappeared will probably be a couple of months on the average; it may be a little less or it may be a little longer. The next thing he will probably say to you is: "I have come to you in good time for treatment; shall I have secondary syphilis?" If you have correctly diagnosed the case he will have secondary symptoms. If that patient does not have secondary symptoms I think in most cases you will correctly conclude that your diagnosis was wrong. I look upon secondary symptoms as the real confirmation of your diagnosis. At what period would you expect secondary symptoms to come on? The period at which secondary symptoms occur is about twenty to forty days after the sore was first noticed. The sore will begin to clear off about the fortieth day. Those secondary symptoms are ushered in partly with some constitutional disturbance and partly with a local manifestation of the rash which you see. Say you have put your patient on mercury with the first diagnosis of a sore, and he has been coming to you regularly, as a patient who is taking that should do, two or three times a week, you ask him how he is. He says, "All right," and that if it were not for the trouble down below he would feel quite well; he has a good appetite and sleeps well. Then there comes a day, say about the twentieth day after the disease was noticed, and you ask him how he is. He says: "I do not know what is the matter with me, but I do not feel at all well; I felt seedy yesterday and could not eat my dinner. And I feel rather seedy this morning." You take his pulse and find it has, perhaps, gone up to 100, and you will find also that his temperature has almost certainly gone up to 100° or 101° F. Ask him if he has a sore throat, and he says he has. You look into his throat, and you see redness like that caused by a cold. You know that that patient is on the eve of getting his local secondary symptoms, and in a day or two from that time the secondary rash will appear. The secondary rash is rather typical. The syphilitic rashes occur to a certain extent evenly distributed all over the body, thus differing very much from many other rashes which have certain points of selection. Psoriasis, for instance, comes on the extensor surfaces rather than on the flexor surfaces, and the same may be said about lichen. The secondary rash of syphilis looks as if someone had put the rash in the family pepper-box and shut your eyes and sprinkled the patient all over with it. But there is this exception, that in three cases out of four you do not get a rash on the hands and you do not get it on the face. So far as the patient is concerned that is rather an important matter, because the patient does not mind a fairly copious rash under his jersey, but if it occurs on his hands and face it is rather awkward for him, and for family purposes when it appears there he is supposed to have an attack of suppressed measles. I think the fact that the rash does not come on the hands and face means nothing more than that those parts of the body are exposed to the air, and the circulation is rather different on them, and perhaps the epidermis is thicker on this account. This secondary rash begins on the abdomen. When the patient has these febrile symptoms, every day look at him and you will find a spot in one part of the abdomen and another in another part of it, and in two or three days from that a few spots on the

chest, those on the abdomen increasing meanwhile in number. At the end of five or six days they begin to appear on the arms and legs, and at the end of a week on the back. So that by ten days from the appearance of the first spot on the abdomen, the patient's body, except the face and hands, will be covered by the rash. What are those secondary rashes which come in syphilis? A French author wrote a volume on syphilis in which he described dozens of separate rashes. I will spare you that, and after all the object of differentiating one rash from another with regard to syphilis is not of much use except in-so-far as it helps prognosis. By this I mean that according to the character of the rash, to a certain extent, so is the severity of the disease which you have to look for in the future. I shall give you only five of those numerous kinds of rash which have been mentioned in connection with syphilis. The simplest form of secondary rash is a roseola. In that condition the whole body is mottled with little patches about the size of the tip of the finger all over the skin. Little scraps of skin are congested or have an erythematous look, and if you look at it a little way off when the patient has got well-marked roséola it looks as if he had the measles. If you feel over the body where there is roseola you will feel nothing. The condition is merely localised patches of hyperæmic skin. If you put your finger on one of these patches and press it, and then take your finger away, in a second or two the blood comes back into it again, and that will show that that red patch is not due to extravasation of colouring matter from the blood, but is due simply to increased vascularity in these little different areas of skin. That is roseola, the simplest of all forms of syphilitic rash. It is generally well marked at the end of a week, and remains there for any time up to two or three weeks. Generally by the end of the third week it has disappeared. When that rash has disappeared and your patient is healthy in other ways, the chances are that he will never see any more of his syphilis: it has gone for good. So when you see a roseola you can give the patient fair hopes that his trouble is going to be but slight. What is the next form of secondary rash? It is the squamous syphilide, syphilitic psoriasis as we used to call it. Squamous syphilis is a degree further than roseola. The skin in squamous syphilis, as in ordinary psoriasis, is not only hyperæmic, but it has so much inflammation about it that the epithelium has been desquamated, so that there is a little scale or scab forming. And if you look at these scabs you find that they consist of *débris* of epithelium, which had been constantly shed from the inflamed patch of skin below, with sufficient sebaceous material to stick it together in the form of a scab, and in that way you will find that the body, instead of being covered with a thing which looks like measles, will be covered with those patches about the size of a threepenny-piece, covered with a yellow scale, and that scale will be found to be desquamated epithelium. That is a fairly mild form of syphilis. But when I see psoriasis I know that if the inflammation has gone on to desquamation, it is a severer attack of syphilis than where there is roseola. But even there the chances are that the patient will not have tertiary symptoms. But the rash is apt to remain for some little time instead of disappearing in three weeks to a month; it is more likely to hold out for two or three months. So in that sense it is more severe. When roseola comes out there is sore throat for the first few days. When the secondary is in the form of roseola, the sore throat disappears quickly, and the roseola does not come back at all. When there is a squamous rash it is not uncommon to have little sores about the edges of the tongue, and I think it is the same sort of scaly desquamation on the tongue as appears on the body; it is not true sore throat, not a congested throat, but these little tender patches which are the eruption showing itself on the sides of the tongue are possibly also on the palate. We have dismissed two forms of secondary rash, what I call the most hopeful forms. But there are two other rashes: they are called the papular syphilis, or a further degree, tubercular syphilide. The papular rash is this: on the body there are little papules forming, and if you shut your eyes and put your hand over the patient's body with a papular rash you feel these little papules. If you are a gardener I may say the lesions are about the size of a section of a small sweet-pea seed, or if you are a sportsman I would say the size of a No. 2 shot cut into two. They are distinctly raised, with little or no tendency to ulcerate on the surface. They are scattered over the body, so that there are several hundreds of them. The tubercular eruption is the same thing, only you get things very much larger. I have

seen, in the tubercular form, lumps as big as the tip of my finger, but never very many of them; they make up in size what they lack in quantity. I do not think there is much to choose between the forms of syphilis which they separately represent. It may be that such a patient will not have tertiary symptoms, but I think it is an equal chance that he will in six months or a year's time, and that there will then be further trouble. Lastly, we come to the worst form of all syphilitic eruptions as a secondary rash, namely, rupia. When a case of syphilis has rupia as the secondary rash you may be certain he is in for a very severe course of syphilis, and he may indeed never really get well; the condition will go from the secondary to the tertiary symptoms, with ulceration of bone, necrosis, and all sorts of troubles. But fortunately that kind of secondary rash is extremely rare. In my out-patients in the skin department here I had hundreds of cases of syphilitic rashes, but perhaps the rupia cases did not come to more than 1 per cent., so when I got one I used to prize it very much. Nearly all the cases of rupia I saw were in sailors who had brought the disease over from some foreign country, having caught it a few weeks before arriving in this country. What is rupia? I will follow the course of a particular spot. On a particular day, say on a Monday, you will see a red erythematous patch. Twenty-four or forty-eight hours after you notice the red patch, you will see there is a bleb or bulla forms, and then the epithelium is raised and it has serum underneath it, which makes it look like a blister. It looks as if the patient had been touched there with a hot iron, but the skin is not tight, you can see there is serous fluid. After the bleb has been there two or three days, instead of being merely serum it is purulent; you see a nasty yellow-looking bleb containing pus, and after it has been there four or five days it breaks and leaves a raw surface where the patch was. On the raw surface the secretion begins to dry, then more secretion is poured out from the inflamed surface underneath, and this mingling with desquamating epithelium, at the end of two or three weeks forms an oyster-shell crust, perhaps a quarter of an inch thick. I have seen them in size equal to anything from a threepenny- to a five-shilling-piece. At the end of about three weeks—it may be more or it may be less—the crust falls off, or you pick it off, and underneath there is a clear-cut more or less circular ulcer. Since rupia is rather a chronic form of secondary rash you will often see on a patient who has had a rash a month or two, lesions in various degrees, here a red patch, here one of the blebs with serum underneath it, and one a few days older with the pus underneath, and then with a broken raw surface. Then you will see a crust dried on the raw surface, and here and there where the crust is dropped off there will be a well-marked ulcer. So much for the secondary rashes; they generally appear about the fortieth day, and the more severe the syphilis the earlier they come, the less severe the later they come.

Now as regards the question of treatment, how shall you treat your case of syphilis? You must treat it both locally, that is to say the sore, and constitutionally. The local treatment of a hard sore consists of soap and water night and morning. When the patient has washed it in that way he should sprinkle on a powder consisting of 1 part calomel and 2 parts oxide of zinc mixed together. Of course before putting this on he should have washed the penis and dried it with a special towel — not the family towel. Having drawn back the foreskin, a little fine cotton-wool should be put over the powder and the foreskin put back to keep in place. I always hold strongly that it is a great mistake to put anything wet or moist upon a hard sore. If you want a hard sore to extend quickly, you have only to put on some lotio nigra or anything of the sort to keep it wet, and so encourage any germs to extend as quickly as they will. I have always found hard sores do much better with dry treatment. Each time you wash off the old calomel and zinc powder put fresh on.

With regard to the constitutional treatment of syphilis, mercury still holds the field. Speaking generally, I am sorry to say one of my greatest difficulties has been I have always been extremely sceptical as to the value of drugs, but I confess I believe mercury has some effect in shortening the attack of syphilis. At any rate I shall not intrude my dislike to drugs upon you. But it is conventional treatment, and you will probably have to adopt it. In administering mercury for syphilis there are at least three or four different ways in which it can be done. It can be done by putting the mercury up in the form of a pill, hydrarg. cum

creta two grains twice a day to begin with. Another form is hypodermic injection of a very small quantity of perchloride of mercury, which is a good form in which to give it. Then there is the inunction of mercury, which is practised at Aix-la-Chapelle, where blue ointment is rubbed by professors thoroughly into the skin. The rubbing in is very difficult to do properly. At Aix the patient has a bath, which thoroughly softens the skin, and when he is in that condition he is dried with a towel and the attendant rubs him with twenty grains of blue ointment. That is done every day, and it is a very good form of treatment. But if it can be avoided I do not like to send my patients to Germany for treatment; I prefer to treat them myself in this country.

Then there is the treatment which was very fashionable twenty-five years ago when I was seeing syphilitic patients, namely the use of the vapour of mercury. Mercury was volatilised with water, and the patient exposed the body to that vapour. In that way a certain amount was absorbed. But it is a little difficult to manage. You have a little cup containing five grains of calomel, and round the cup outside is a saucer with two ounces of water and a spirit lamp underneath, which was so arranged that the steam volatilised with the mercury. The patient sat on a cane-bottomed chair and had a mackintosh towel round his shoulders. He struck a match and lit the lamp, then lighted his pipe, got a newspaper, and sat there hoping things were going on all right. Having sat there a few minutes he would find the thing was out, and that a lot of time had been wasted. One patient complained that he had not sat there very long before he found his night-dress on fire!. So you see the treatment is a little complicated. If I had time I would enter into further detail with regard to the treatment of syphilis, but anyhow I have now suggested three methods of administering mercury. Certainly the easiest and most satisfactory method is to take the mercury by the mouth. I do not think anything answers better than the hydrarg. cum creta, moderate doses. Directly I have made up my mind that a case is syphilis I put the patient on two grains of hydrarg. cum creta twice a day, and continue that for a fortnight. If at the end of a fortnight I find he has no tenderness or other affection about the gums, I would give the patient a little more, increase it to three grains twice a day, or give that quantity three times a day. As soon as the gums are a little bit touched by the mercury, decrease your dose. The treatment with small doses may be continued three to six months, but has to be most carefully watched.

May 31st, 1909.

A DEMONSTRATION OF CASES OF NERVOUS DISEASE BY MEANS OF THE CINEMATOGRAPH.

At the Medical Graduates' College and Polyclinic.

By WILFRED HARRIS, M.D., F.R.C.P.,
Physician to Out-Patients, St. Mary's Hospital, and to the Hospital for Epilepsy and Paralysis, Maida Vale.

GENTLEMEN,—Some of you may possibly have seen some pictures taken by this method which Dr. Campbell Thomson showed at the Royal Society of Medicine some time ago. He is the first in this country who has utilised this method for the demonstration of clinical cases. Some cases have been kindly photographed by the Urban Bioscope Co. for me by this method, and they have arranged all this for me, and I think you will agree that they show very well the modes of progression of patients who have altered gait in consequence of some nervous disease. Not only will it show different forms of gait, but cinematic photography as applied to medicine can be made to show other things, such as the responses when testing the different reflexes—ankle-jerks, knee-jerks, plantar reflexes. It will also show the movements of the eyes, such as nystagmus, paralysis of the ocular muscles, and various facial movements, paralysis of shoulder muscles, etc. I think it is a method which has a great future before it for the teaching of medicine. Perhaps it will have more value for teaching in cases of nervous disease than in general medicine, but it can be used for general medicine. Cases of pyloric stenosis, for instance, can be shown by it, for it will show the shape of the dilated stomach, and the movements of peristalsis.

The cases of which I shall show you the illustrations to-day are not arranged in any definite order, because the films were put together haphazard, and I have not yet had them changed because we shall make a series of types of cases; Dr. Campbell Thomson's and my own cases will be put together to make a typical set. These pictures are taken by means of the bioscope camera at a rate of sixteen per second, and they will be shown at about the same speed. That is not the highest rate at which these films can be

taken, for they can be taken at as rapid a rate as thirty-two per second. For such things as horse-racing that high speed is used.

The first case is one of tabes, and you will see that the patient has no ataxy at all. He has Charcot's disease of the left hip-joint, and I have included him among other cases of tabes for that reason. You will be able to see considerable swelling over his left hip. As he comes forward with his eyes shut you will notice that he sways a little, but he can stand without falling with his eyes shut. The next case is one of spastic paraplegia from combined sclerosis. The man has weakness of both legs, more of the left than of the right, and you can see him walking in a stiff way, unable to bend his knees, and consequently scraping the ground with his left foot as he goes. His arms are all right. I shall show the same man soon in relation to the demonstration of reflexes.

The next case is one of infantile paralysis. This little boy has very marked wasting of his left lower extremity, the thigh and leg, and he walks throwing himself on to his left hip each time he takes a step, and that is because he has no quadriceps extensor. I shall ask you to compare that gait with one which I shall show presently, in which there is no wasting of the thigh, only wasting of the leg. In that case there is a dropping of the foot, but no wasting of the thigh, and he does not throw himself from one side to the other.

The next is a case of hysterical paralysis. The patient shows a curious gait which we cannot put down to any known form of nervous disease. It is a tripping gait: she takes very short steps and keeps her knees bent. It is a case of pure hysteria; there is no organic lesion. One cannot imagine any reason for these short steps.

The next case is one of peroneal paralysis, and I shall ask you to compare this case with the boy suffering from infantile paralysis. He has a dropped foot, and does not throw himself on to his hip because his thigh is all right. He got this injury by a severe crush. He was wound up on a lathe, and his leg was crushed against a furnace door, and besides having his shoulder crushed he got this condition.

The next is a case of paralysis agitans of a very interesting type, because her gait will strike you as being more that of a case of hemiplegia on the left side. There is a scraping of the leg along the ground, but she does not swing her arms as she walks. There is very marked rigidity, not only of the trunk muscles, but also of her face, and later on you will see the rigidity of her face as she talks; there is a want of expression of the facial muscles. The chief interest about this case is that it is such a marked hemiplegic gait. In a later picture you will see the tremor of her hands.

The next case is a man who has the Landouzy-Dejerine type of myopathy; that is to say, the facio-scapulo-humeral muscular atrophy. He has extreme atrophy of the muscles of the upper limb and of the thigh, very little of the forearm or of the muscles below the knee; the serratus magnus is completely paralysed on both sides, the trapezius completely on both sides, the levator anguli scapulæ paralysed on one side. There is extreme lordosis, and he has the gait which was christened by Ross, of Manchester, the "Grand Ducal swagger." He has no quadriceps extensor, and he has to throw himself on to each hip in turn. Owing to the lordosis, and the fact that the stomach is thrown forward, he gets this characteristic swaggering gait. It differs from pseudo-hypertrophic paralysis in that there is no pseudo-hypertrophy: but it resembles it closely in the distribution and in the atrophy, the muscles of the upper arm, the biceps, triceps, and some of the back muscles, and also differs from the pseudo-hypertrophic type in that it comes on later in life; it affects both sexes, and especially affects the facial muscles. You will see in a later picture that the facial muscles are quite powerless. He is trying in this picture to close his eyes and purse up his lips, but he cannot. In these cases of facial palsy the child may be born with inability to suck or to close its eyes, but there may be no atrophy of the muscles of the trunk or limbs until ten or fifteen years of age. But all the same, they can be recognised as an early stage of Landouzy-Dejerine myopathy. Notice how his shoulders are hanging. For years he attended my out-patients at St. Mary's Hospital, but now, having no means of support, he is in Paddington Infirmary.

The next man is one with paralysis agitans, but quite different in appearance from the woman you saw just now. You will see that he walks perfectly freely, and he is fond of saying that he will walk anybody down the Bayswater Road for a wager. That is not what you would expect in paralysis agitans, but all the same it is such a case. He has

typical tremor of his left arm. It does not show very well on the film. He will come forward and stand, and I can tell you that the shaking did really become evident. He has commencing rigidity of his arm, so that various movements of it are lost, and he has the characteristic facial appearance of the disease. He complains that the arm stops when he tries to black a boot or do anything requiring muscular force. He has none of the rigidity of the limb-muscles or of the muscles of his shoulder or arm. He swings his arms freely as he walks, and his gait is good and free; there is no shuffling. I have not in this film a typical case of paralysis agitans, but Dr. Campbell Thomson has photographed a very typical example.

The next case is one of very advanced tabes. You could not get a more typical case of what is called the "prancing" gait of tabes. He is so ataxic that he cannot even stand alone, and therefore it is necessary to have someone to help him. He throws out a foot and it comes down with a jerk, and in walking he takes a fairly wide base. He has considerable ataxy, and you will see him watching his feet carefully. He has considerable difficulty in turning round. There is no muscular paralysis. The foot is held up well and there is no dropping, but he rather comes down on the heel as a rule.

The next is a case of diplegia due to infantile damage to the brain, probably ante-natal in this case. It is a case of polio-encephalitis, or damage to the grey matter of the cortex, and when it causes paralysis of one or other side, or both sides, as in this case, it is known as diplegia. Sometimes this disease will strike only the frontal lobes, and may not cause any motor paralyses at all, and that child will be an idiot or an imbecile, but perhaps will not be paralytic. In the cases where the motor convolutions are struck by the disease the child will be paralytic, and the mental condition will not be so damaged as in the case of frontal polio-encephalitis. The mental condition is sometimes quite good when the disease is limited to the motor region, but in the majority of even the paralytic cases the mental condition is not perfect. These subjects are liable to have fits, and generally they are backward children, sometimes imbecile too. This particular child has paralysis down both sides, and her age is now about 8 years, and yet she has only been able to walk alone for about twelve months. In addition to the weakness and the difficulty in balancing herself, she has spontaneous twisting movements of the arms, head and legs. She has torticollis and there are spasmodic movements of the head, irregular inco-ordinate movements of the head, arms, legs and body, a condition sometimes called "bilateral athetosis." The athetosis may be limited to one side, and it often is so limited in infantile hemiplegia. Sometimes the movements are much more choreic in type, and such a case as this is sometimes called "choreic diplegia."

In the next film you will see the case of spastic paraplegia back again, and it is for the purpose of showing the method of testing the reflexes. The first is ankle clonus. If the Achilles reflex is very lively the movement is likely to be repeated several times, and if it is continued it is known as ankle clonus, which is practically pathognomonic of organic spinal lesion of the pyramidal tracts. I have another film showing pseudo-clonus or hysterical ankle clonus, in which there is no true lesion of the pyramidal tracts, either in the brain or the cord, and yet the man has very violent jerky movements of his foot. In that case the clonus comes on spontaneously, without anyone touching the foot at all. He had flexor plantar response, and under stimulant and moral treatment he is improving. The left leg is the stiffer and the more spastic, and that is the one which shows the ankle clonus best. Next we try the plantar reflex, using a pin and scratching the sole of the foot with it underneath the ball of the great toe. On the right side, the less spastic leg, one does not get a very good type of extensor plantar reflex, but in the left foot we get it very well. And it shows this peculiarity, that in the left foot on scratching the sole of the foot inside, under the ball of the great toe there is a flexor response, whereas on scratching it on the outside there is extensor plantar. That is a form of extensor plantar which is sometimes seen. The extensor plantar can be elicited in other ways than by scraping the sole of the foot. There is a reflex described by Schaffer in 1899, and in 1904 was re-discovered in America by Dr. Gordon, who would like it to be called the "paradoxic reflex." The method of eliciting it is to press firmly the flexor muscle at the back of the calf, and with your thumb exert forcible pressure on the back of the calf. The result will be an extensor plantar

reflex. You can produce it in another way, as Oppenheim showed. He uses the stiff handle of a percussion stethoscope, and presses the handle firmly along the skin and deeply into the muscles on the inner aspect of the tibia. That also will illustrate the extensor plantar reflex in these spastic cases. It means that the skin area—and the muscles even share in it too—in which stimulation causes extensor plantar response, may extend over a much wider area than just the skin of the sole of the foot. Babinski himself early recognised this. Sometimes stroking with the hand, even on the thigh, may induce the extensor plantar reflex. This mode is known under the names of these gentlemen: Oppenheim, Schaffer, Gordon. There is also another reflex which this patient shows, but it is not very common in these spastic cases. It is described by Bechterew, and he produced it by tapping, with a percussion stethoscope, the extensor tendons on the dorsum of the foot, rather on the outside. Tapping those in the normal person either produces no reponse at all, or, if there is one, it is extensor. But in spastic paraplegia it often produces the opposite result, namely, flexion of the toes.

The next picture is also put in to illustrate one of the reflexes: Babinski extensor plantar and ankle clonus. It is interesting to me because the method of stimulating the sole of the foot to cause extensor plantar response starts an ankle clonus itself in this case. I do not use pressure, but simply scratch it with a pin. This photograph is taken in the ward at Maida Vale. The reflex indicates a lesion of the pyramidal fibres, but it starts an ankle clonus in itself.

We now come back to the case of Landouzy-Dejerine myopathy. This film shows the facial palsy and the paralysis of muscles about the shoulder. The patient will try to close his eyes and mouth, but, as you will see, there is very little result at all; the whites of the eyes roll up, but that is all. He has no power over the zygomatici or risorius, or orbicularis oris. The lips in his case have been paralysed from birth, and he said his mother told him his face had always been so, though he did not begin to develop atrophy of the muscles of the trunk until he was about twenty years of age. It is a very chronic disease and slow in its progress—slower than pseudo-hypertrophic paralysis. I watched him regularly for five years, and there was but little change in that time, though the patient himself thought he became a little better. He is now obliged to go into the Paddington Infirmary. You will be able to clearly see the atrophy of the trapezius and of the serratus magnus, and the left scapula is placed very much higher than the right. There is absence of the levator anguli scapula on the right side.

The next patient, a woman, shows some of the signs of ophthalmoplegia. It is not complete. She has power over the superior recti and over the external recti, but there is bilateral ptosis and she has palsy of the inferior rectus on the right side. Owing to the double ptosis she has over-action of the frontalis on both sides, so she has a deeply lined forehead, from the frontalis trying to help the weak levator palpebræ.

The next is a lady with the hemiplegic type of paralysis agitans. She shows the facial rigidity of paralysis agitans very well. She is counting from 1 to 20, as you will see from the movements of the mouth, and she is holding up her hands to show the tremor in them. This is sometimes called the Parkinsonian mask, from the fact that Parkinson described this peculiar aspect of face.

The next case is one of syringobulbia. It is the same disease as syringomyelia, but affecting the upper regions. It is affecting the hypoglossal nucleus and two sixth nuclei, so that he has hemiatrophy of the tongue and has difficulty in moving his eyes to the right. When he tries to do so you will notice that he has violent nystagmus towards the right. When he looks to the left there is no nystagmus. With regard to his sensations, he has a very large area of analgesia, which, of course, I cannot show in this way. It extends from the back of the head down the neck, escaping the arm, and down the trunk and thigh to the right foot.

The last picture but one represents the pseudo ankle clonus which I mentioned earlier. There is a violent spontaneous clonus going on without any attempt being made to elicit it at all.

The last picture shows two children—rickety twins—who are at St. Mary's and have a curious mode of progression, shuffling along on their glutei. They amuse themselves sometimes by racing each other along the floor.

May 31st, 1909.

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POST-GRADUATE LECTURE

ON

THE USE OF THE CYSTOSCOPE.

By E. STANMORE BISHOP, F.R.C.S.,
Hon. Surgeon Ancoats and Jewish Hospitals, Manchester.

GENTLEMEN,—When empty the urinary bladder may be looked upon as a cleft in the tissues between the peritoneum above and behind and the pubes below and in front. All the urinary apparatus is extra-peritoneal, and may be reached extra-peritoneally from the upper pole of the kidney above to the lower pole, the tip of the urethra below. The bladder cavity itself is surrounded first by a mucous membrane, then by a submucous layer of loose connective tissue which allows the lining membrane to have free movement upon, and anything but a close attachment to, the next or muscular layer. The advantage of this is that when that muscular wall contracts it does not necessitate equal contraction of the mucosa. This is puckered up into folds, which present to the eye through the cystoscope a very misleading appearance unless the examiner is prepared for it. This is the case everywhere except at the trigone, a triangular space at the base, into the angles of which three tubes enter. Over this area the two layers, the mucous lining within and the muscular layer without, are far more firmly connected, whilst below the muscular wall is a plane of strong connective tissue which supports and keeps it always in the same position both absolutely and relatively to those openings. That the connection of the mucosa and muscular wall is not even here absolutely intimate is shown in cases of hypertrophied prostate. The upper edge of the prostate lies normally just below the trigone, but when that gland enlarges, since it cannot enlarge downwards and forwards in consequence of the rigid resistance of the triangular ligament, it slowly separates the

trigonal mucosa from the muscular wall and projects beneath the mucous membrane into the bladder cavity. It is owing to this that in suprapubic prostatectomy, when once the bladder is open above it is only necessary to divide the mucous membrane over the projecting prostatic growth to come down at once upon the prostatic tissue, and by keeping the finger close to that tissue to be able to enucleate the tumour without in any way damaging the muscular wall.

Another result of the loose connection of the mucosa, although it cannot be called an advantage, fairly often seen in elderly persons, especially in those who have suffered from stricture or any chronic impediment to the outflow of urine, depends upon this fact: I mean sacculation of the bladder. These saccules, sometimes very large, are composed only of mucous membrane. The effort to expel its contents causes the muscular fibres of the vesical muscular coat to hypertrophy. Their tonic contraction slowly induces degeneration of these fibres, which are replaced by fibrous tissue; these bands of connective tissue have no power of relaxation, and their persistent contraction —the contraction of scar tissue—causes them presently to stand out as rigid bars beneath the mucosa. The muscular fibres of the bladder are, as is well known, arranged in three layers, but these layers are not evenly distributed over the entire circumference; weak places occur, which are shown and accentuated by any marked increase in the intra-vesical tension, and at these points the mucous layer, being free to move, is forced outwards between the muscular fibres as a kind of hernia. Such a bladder is known as a sacculated or trabeculated bladder, the trabeculæ being these hypertrophied or degenerated muscular fibres; the appearance of this kind of bladder through the cystoscope is very characteristic.

I have spoken of the misleading appearance of the mucosa in a bladder which is not distended. Normally, and when a healthy bladder is full, the lining membrane lit up by the cystoscopic lamp has the sheen of mother-of-pearl and appears to lie flat upon its surrounding muscular wall. Over its surface can be seen a few—a very few—red arterioles, very fine and just visible. In cystitis these vessels increase in size, and many previously invisible are now seen; the whole surface loses some of its polished appearance and looks reddened. But when cystitis has lasted for some time the folds into which the mucosa naturally falls when the bladder is contracted become swollen and stiffened; they do not open out again with the same ease. Besides, the irritation within, following Hilton's law, sets up a tonic spasm in the muscular wall, which remains contracted over the mucosa; if the bladder has not been fully distended, even though perfectly healthy such folds being left strongly suggest cystitis, especially that form of cystitis which is not general but patchy; it is a great advantage therefore to be able to alter the amount of intra-vesical tension in such cases whilst the cystoscope is still in the bladder; with the ordinary instrument [shown] this is not possible. The cystoscope must be withdrawn and a catheter introduced, through which more fluid may be added; this may be more than sufficient, and in any case the attention of the observer is taken off from the part he wishes to follow; the only guide to the necessary amount is then the patient's own sensations. It is, however, curious to notice in this connection that even under chloroform the bladder resents any over-distension, and shows its effect by unconscious moans and movements of the lower limbs. But with this later form of cystoscope [shown] you will see that through a narrow tube on the concavity of the instrument fluid can be added or withdrawn whilst yet the cystoscope is *in situ*. The examiner can then watch the unfolding of normal uninflamed folds, or note their persistence in cases where they are inflamed, and therefore stiffened.

When a novice has passed a cystoscope into the bladder, what does he see? Simply at first a lit-up space, and it is only after some practice that he begins to recognise the geography of the place. There are three things that he should first of all try to get clear in his mind; first, the internal orifice of the urethra, and next the two ureteric openings, one at each posterior angle of the trigone.

The internal urethral orifice cannot itself be seen, since the instrument itself lies in and passes through it; but what the examiner does see is a straight-edged patch of chocolate red. This is the inner edge of the urethra, and the appearance is produced by the light shining through the vascular mucous membrane around it. If one looks at a cystoscope is evident that the prism through

which the rays of light pass to the eye, and which is therefore the eye of the instrument, is placed at some distance behind the lamp which emits those rays, or in other words supplies the light by which any object observed is seen. If the prism is just within the urethra, the light will already be in the bladder and will shine through the vascular ring of mucous membrane surrounding that orifice, and produce the impression on the observer's eye of a dark red area. This is the first thing to locate; when this is seen the position of the prism is known; it lies immediately beneath the edge of the internal urethral orifice. At this time it is quite easy to rotate the instrument, since its beak, bearing the light, is free inside the bladder.

The line produced at the edge of this area should then be observed; if straight, or slightly lobed, it is normal; but if curved strongly upwards, either in the centre or at the sides, it will denote in the male some enlargement, and therefore encroachment upon the bladder space of the prostate gland; the amount of curving will be a guide to the size of the enlargement, and its irregularity to the shape of that hypertrophy; as no prostate exists in the female this line in women is never largely curved in this way.

The ureteral orifices are much more difficult to locate, partly because in a healthy bladder they are extremely small, and more like short, fine, red lines than any gaping tube end. For easier demonstration, and therefore especially for those who are commencing the study of cystoscopy, a great advantage is gained by previously injecting the patient subcutaneously with a drachm of the solution of indigo carmine; this has no deleterious effect, but it colours the newly secreted urine blue, and the blue jet can easily be seen at its emergence from the ureteral mouth, to which it thereby draws attention before it mixes with the clear boric acid solution which fills the bladder. The colour begins to appear in about forty minutes after injection; any delay in the time taken for its appearance indicates renal incapacity, and the difference in the time between the two sides will show which kidney is doing the most work and in the most efficient manner; failure to appear at all on one side will indicate either total inefficiency of the corresponding kidney or entire blocking of the ureter on that side.

The condition of the ureteric opening is a point of much importance. Normally it is a faint red line, which pouts inwards towards the bladder just before and during the escape of a jet of urine from its correlated kidney; at such a time it becomes slightly rounder and more prominent. When ureteritis is present due to the passage through it of irritating pus or crystalline material the area immediately around shows signs of inflammation, which may vary from a leash of fine vessels which spread outwards from the ureteric opening as a centre to great swelling and deep purplish discolouration for some distance around.

It must be remembered that inflammation of the bladder is very frequently limited in extent, and that the existence of cystitis does not necessarily involve the participation of the whole internal surface; one side or even a small patch may be greatly inflamed, whilst the rest may retain its normal appearance.

The changes observed in the ureteric openings are very instructive, inasmuch as they furnish evidence of the kidneys and ureters above; but it is necessary to be certain that these changes are actually in and not merely near the ureteric openings before any inference is drawn from them, since certain ulcers of the bladder itself are found sometimes close to these openings, from the presence of which no such inferences can be drawn; such are the simple solitary ulcer and the single tuberculous ulcer.

The ureteric opening may be elongated and its lips swollen and congested. Such an appearance denotes something distending the pelvis of the kidney above; it may be tubercle, calculus, hydro- or pyonephrosis. It is useful in calling attention to the kidney above, and in determining the side affected when other symptoms are present which show disease, but do not themselves locate it.

The lips of the ureteric opening may be rounded, swollen, everted, eroded, or even ulcerated, and the immediate area around reddened. This appearance denotes that caustic alkaline urine is entering the bladder through this particular ureter; such alkaline urine may be due to tubercle, or to calculus. The points which differentiate the two cystoscopically are:

Tubercle.	Calculus.
A thick edge, sharply cut.	A tendency to eversion of lining mucosa.
Orifice patched with extravasations.	No such patches.

Tubercle.	Calculus.
Opening dragged outwards.	Opening in normal position.
Surface ulceration of bladder wall, which may be extensive.	No extensive surface ulceration.

In the earlier stages of both pus is emitted from the affected side with the urine at a more rapid rate than the normal, whilst the healthy kidney may be sluggish in its action; the diseased organ is evidently stimulated to more active secretion than that on the opposite side.

As time elapses, however, the position is reversed; the rapidity of the jets on the affected side becomes less as the kidney becomes more and more disorganised, whilst the unaffected kidney is stimulated by the exigencies of the organism to do more and more of the excretory work. This of course is more essentially the case with the tuberculous kidney; the efflux from the affected side becomes more and more sluggish and the pus thicker, until at last it may even resemble the pressing out of macaroni. The kidney has then become functionally useless.

June 7th, 1909.

Pericardiectomy.—Parlavecchio states that he has found sixteen cases on record in which autopsy revealed congenital absence of the pericardium or mere rudiments. In none of the cases had there been noticeable disturbance from the lack of the pericardium, except possibly in one case with mitral stenosis. Amerio has experimented on rabbits to learn the effects of complete removal of the pericardium, which he found feasible, and Parlavecchio reports a series of recent experiments on dogs, the results of which confirm the findings of Amerio with rabbits, although pericardiectomy is more dangerous for dogs than for rabbits. The functioning of the diaphragm does not seem to suffer if the phrenic nerve on one side is left intact. It is important to refrain from injuring the auricles and large vessels, and even from touching the right wall of the pericardium for fear of injuring the other phrenic nerve or the other pleural cavity. The surgeon may therefore feel justified in removing almost the whole of the pericardium in malignant disease or in chronic pericarditis resisting other measures. If pleuritis results this is much easier to cure than pericarditis.—*Journ. A. M. A.*, vol. lii, No. 20.

THE RESULTS OF RECENT RESEARCH ON CERTAIN DISEASES.*

By F. M. SANDWITH, M.D., F.R.C.P.,
Gresham Professor of Physic.

For the satisfactory and complete study of a disease three things are necessary for the student: he must see the disease in a living patient, he must see after death the effects that that disease has produced in the patient during life, and he must study all that is recorded in literature on the subject. But how can the scientist obtain that exact information which is necessary, both to tell him how the diseased organs are being affected and also what the result of certain drugs or other treatment has on these organs? There is one method, and one method only, by which such accurate research can be carried out, and this is by experiments on living animals. For instance, the existence of a minute parasite in the blood is the cause of certain fevers, and when such a parasite is suspected of being the cause, experiments on living animals are often employed. The material containing the parasite, that is, the blood, is injected into an animal which is found by experiment to be susceptible to that particular poison, and if the injection sets up the disease in a series of such experiments we have proof positive that the suspected parasite is the cause of the fever.

It would be abhorrent to us all if we believed that such experiments, necessary for saving life and pain in man, were attended by great pain in the animal, but let us be assured that this is not the case, at least in the present day in this country. Quite apart from the question of humanity the experimenter loses the value of the experiment should the animal be put to great pain, and the utmost caution is exercised to limit that pain by anæsthetics and other means, to such an extent that we may say that in not 1 per cent. of the animals experimented on has any pain, worthy of the name, been inflicted. The strict application of the law has limited the experiments on living animals to those few only who are efficient and who are serious men of science; the law is not evaded and inspection is careful and thorough. But there

* A lecture delivered at Gresham College.

are those who will tell you that these experiments are useless, that observation by the bedside should be sufficient to discover the cause and treatment of any disease. Those who make such statements must be phenomenally ignorant of the complexity of disease, and also of the history of medicine, for before the experimental era dawned no great discoveries were made in the study of medicine.

All treatment, however carefully chosen, is in the nature of an experiment, for none can know the exact effect of any treatment or drug on any individual patient until he has tried it. A drug may suit ninety-nine people but be injurious to the one-hundredth because of some personal idiosyncrasy. Our remedies are used with the greatest certainty of success when they have been repeatedly tried on living animals and their exact effects have been watched.

We are all proud of our great countryman Harvey, who discovered the circulation of the blood in 1628 and reversed all previous theories in medicine. It was a discovery which may be called the foundation stone of all medical knowledge. Before it was made our ancestors were but floundering in a bog of theories and expectations. But Harvey laboured for years at systematic experiments on living animals, and revealed the fact that the blood circulates from the heart to the limbs and back again to the heart. Since his day all the greatest discoveries in medical and surgical science have been brought to light by such experiments, and I want to bring before you in these lectures the results in some diseases where the facts are striking and the saving in human life and in suffering are greatest.

Remember also that it is not only man who has profited by knowledge gained by experiments. The ravages of glanders, animal tuberculosis and anthrax, to mention only a few, have been controlled and have saved thousands of poor beasts from terrible suffering, and at no distant date these experiments may help us to stamp out these scourges altogether.

To-night I want to tell you of Malta fever, a disease little known in this country, but in which those of you who have relations or friends serving their country abroad should be interested.

Sir David Bruce, of the Royal Army Medical Corps, has devoted much study to this disease, and in writing of it he says: "I would draw your attention to the prevalence of this disease among our soldiers and sailors in Malta, in order to impress upon you the importance of this disease to the State. Among the soldiers, who average as a rule about 8000, there is an average yearly incidence of 37·6 per thousand, or 312 admissions to hospital every year for Malta fever. Among the sailors there is an incidence of 28·55 per thousand, or about the same number of admissions to hospital as among the soldiers. Now as the average duration of this disease may be put down as four months, it means that 624 soldiers and sailors are in hospital 120 days, which makes 74,880 days of illness. What an amount of personal suffering and loss to the State this sickness and invaliding entail it is impossible to estimate, but the mere pecuniary loss must be very considerable." This was written in 1906, and we shall see later on what recent discoveries have brought about.

Malta fever runs a long, indefinite course, lasting many weeks or even months, and although not many people die of it (only about 2 per cent. of those attacked), it causes long suffering and discomfort, and renders a man unfit for work for months, sometimes for years. The complications are more serious than the actual disease, rheumatic affections of the joints, such as the hips and knees or shoulders, being common after-effects, or affections of the respiratory organs, bronchitis, pleurisy, or pneumonia.

The illness has been known on the sea coast towns of the Mediterranean for hundreds of years, but lately our knowledge has become definite and precise, with the results which I will relate to you. We may talk of the intellectual development of man as, first, a period of ignorance or want of knowledge, secondly, a period of latent knowledge, and then a period of specialised and accurate knowledge. This disease, like most others, has gone through these same stages. First there was ignorance about it, nobody knowing what it was and confusing it with malaria and typhoid fever. Later the micrococcus was discovered, that is, the parasite in the blood that gives rise to the disease, and that may be described as the period of latent knowledge. People said that is the micrococcus which must get into the body, but how does it get out of one person's body and into another person? That could not be satisfactorily answered until lately, but now we may say we have special know-

ledge on the matter; we not only know that there is a micrococcus (and that was known some twenty years ago), but how it gets out of one human body and enters into another. That is a little further than we have got concerning many bacilli.

Let us look at the different names which are given to the disease we are discussing this evening. It is called "Malta fever" because it is connected with Malta so much. It was called "Mediterranean fever" because it was thought to be chiefly connected with the coasts of the Mediterranean sea. It was also called "Gibraltar fever" and "Rock fever" because Gibraltar is known as the "Rock." Again, "Neapolitan fever" because it was found in Naples; it has been called "Cretan," "Cyprus," "Danube," and "Levant fever." The term "undulant" has also been given to it because, as you may see here, the typical fever chart shows a series of undulations or waves.

It is an endemic fever sometimes becoming epidemic. It is of long, indefinite duration, with a tendency to long wavy relapses, characterised by constipation, profuse sweats, anæmia, debility, neuralgia, and sometimes rheumatic sciatica and swelling of joints. The disease is dependent on a specific microbe, but is not directly contagious.

Now as to the history. In the history of ancient medicine everything seems to go back either to the Chinese or to Hippocrates. This time it is Hippocrates who wrote about 400 B.C. of long fevers occurring on the coast of Greece—and it is still very prevalent in Greece—with as many as four lengthy relapses, and on one occasion death on the hundred and twentieth day.

But it was not until 1859 that Malta fever was first described as a specific illness. In 1886 Colonel Bruce found a special micrococcus and named it after the island of Malta—*Micrococcus melitensis.*

As to its distribution, I have given you the names of some of the places which have given a synonym to the disease. There are a few others, mostly seaports: Sicily, Sardinia, Constantinople, Tunis, and Algiers. So far we have justified the name "Mediterranean," but it spreads a long way from there. It is on the Red Sea coast, at such places as Suakin and Zanzibar, also the Punjab, Simla, Delhi, Agra, Allahabad, Assam, Hong-Kong, Porto Rico, West Indies, and the Philippine Islands—a fairly big geographical range. It is only natural that I should not wish to exclude Egypt when I am touching on geography. This fever was unknown in Egypt until I found a case in November, 1883, in a young English lady who had travelled leisurely from England through Italy on her way to Cairo. The symptoms of her disease I found to be similar to those which I had studied in cases in Gibraltar and Malta. Quinine in large doses had no effect on the temperature, which lasted one hundred days. There have been cases also in the Sudan, beyond Khartum, and one coming from the Blue Nile I will describe to you later. One man contracted this fever on the White Nile, and it has been found at Kassala, in the Sudan, and among the Abyssinians. Lastly, there is one interesting case of this fever in a man who had never left England. He was a gunner, who died at Dover on the hundred and twenty-second day of his disease. The statistics of the British Navy for the three years ending in 1903 gave 831 cases in the Mediterranean, of which 620 were attributed directly to Malta, 30 to Gibraltar, 30 to Corfu, 3 to Alexandria, and the remainder to other ports. Thus the British Navy suffered tremendously, and they got the disease chiefly at Malta. This is one of the things which troubled us with regard to the causation of this illness. We may send our patients for a sea voyage—and we cannot conceive a healthier life than in a man-of-war—and yet the men, and especially the naval officers, suffered terribly from this fever. We could not tell how this was, and the fact that the officers got the disease more in proportion than the men also perplexed us. Some fevers are conveyed by the bites of mosquitoes; could these insects be the cause here? But officers are better protected from mosquitoes than the men are, they had better food than the men, and yet they were more attacked by the disease.

When improved sanitation was introduced in Malta the disease was not eradicated. On the other hand, improved sanitation appeared to effect a cure in Gibraltar, where the well-known "Rock fever" diminished and actually disappeared completely in the year 1904. This occurred shortly after certain changes in the sanitation of Gibraltar were carried out, and it was not unnatural, therefore, to assume that the diminution of and disappearance of the disease were due entirely to the public health measures which were adopted. For instance, the

main sewer of Gibraltar was lengthened, and greater attention was paid to the drainage of the houses, to street paving, and to scavenging. There was stricter supervision of food and milk, and, most important of all, there was the formation of reservoirs in the rock for supplying all the inhabitants with pure filtered rain water. They have rain at special times of the year, and they catch it in the large reservoirs in the rock for use in the dry season.

But Major Horrocks, R.A.M.C., pointed out that twenty years ago the milk supply of Gibraltar came from the goats which had been imported from Malta; later, difficulties arose about importing these goats, and now goats are brought from Spain into Gibraltar, or else they are bred locally on the Rock itself. The lesson to be learnt from that is, that it was not the improved sanitation which was responsible for the change, but the alteration in the milk supply which caused the disease to disappear.

In 1904 a Royal Commission was appointed by the Royal Society, at the request of the Admiralty and the War Office and the Colonial Office, to inquire into the causes of Malta fever. Sir David Bruce and others have described the happy results of the Royal Commission which worked for three years at Malta. The results of its labours add another feather to the cap of the scientific officers belonging to the Army and Navy, because it is chiefly due to their work that the discovery which I want to tell you about has been made.

Fortunately for us, monkeys, like man, are susceptible to this disease, so that the Commission could first of all make quite sure that the *Micrococcus melitensis* is the true cause of the fever. If a monkey is fed or injected under the skin with cultures of this parasite it suffers from precisely the same symptoms that man does, and in his blood the same parasite can be found. It was important next to know how the micrococcus entered the body from one individual to another, and many experiments were made on monkeys to clear up this point, with the result that it was proved that infection takes place by food or drink. A single drink of milk, containing only a few of the parasites, almost invariably gave rise to the fever.

But, besides the monkey, some of the laboratory animals, such as the rabbit or the guinea-pig, could be forced to take the infection by various expedients, such as, for example, intra-cerebral inoculation. The Royal Commission examined various animals, and among them the goat. The goat is very much in evidence in Malta and supplies practically all the milk used, for there are practically no cows on the island. Flocks of goats in charge of a goat-herd are driven through the streets of the town, and this is also the case in the other places I have mentioned. They live in the streets by day, picking up a scanty living on the garbage of the rubbish heaps, on every sort and kind of food, and are shut up in pens at night. They are milked at the customer's own door, who thinks he is thereby sure to get pure milk, and prefers this method to buying his supply in cans at a shop. The Commission originally had very little hope that the examination of goats would yield any result. However, as a matter of routine, several goats were inoculated with the microbe and the result was watched. There was no rise of temperature and no other sign of ill-health. But in a week or two after inoculation, by the Widal test, it was found that the inoculated animals were suffering from the fever. Even then the goat seemed such an unlikely subject for the elucidation of Malta fever that the observation was scarcely continued. Nothing more was done for several months, when by accident the matter came up again, and it was decided to repeat the inoculation experiments. A small herd of goats was procured for the purpose, and, as would be done by every scientific person, the blood was examined before any experiments were made upon them, to make quite sure that the animal was in a healthy condition. To the surprise of the various members of the Commission the blood of these goats was found to react naturally to the agglutination test, which means that the animals, although apparently healthy, were all the time suffering from the fever or were convalescent from it. This astonishing discovery, of course, led to further examination, and to the discovery that in the blood and in the milk of goats could be found the *Micrococcus melitensis*; that is to say, that the animal which was intended to be the medium of the experiment was found to be already suffering from, or had suffered from, this disease.

Some thousands of goats in Malta were then examined, and the great discovery was made that 50 per cent. of them responded to the serum test,

and actually 10 per cent. of them were secreting the microbe in their milk. Monkeys fed on milk, from an infected goat, even for one day invariably took the disease. It was known that monkeys were susceptible, now the further fact was discovered that monkeys got the disease through the alimentary canal, and they got it from the milk of goats which contained this microbe.

At this time there was an important experiment, though an unintentional experiment, on the drinking of goat's milk by man. This was the case of a certain steamer called the "Joshua Nicholson," fully described in the Reports of the Commission. In 1905 this steamer shipped sixty-five goats at Malta to export them to America. I need not tell you that the captain and the crew drank the milk of the goats on the way over, and they drank it in large quantities, because sailors do not usually get fresh milk on board a ship. The result was that everyone who drank the milk was struck down by Malta fever. Sixty of the goats were landed—five of them having died on the voyage—and when they were examined thirty-two of them were found to react to the agglutination test, and the microbe itself was successfully isolated from the milk of several of these goats. This is a very convincing test, and here is another one reported the other day from Rosaires on the Blue Nile.

An Englishman who had been stationed at Rosaires for a year travelled from the Sudan straight to England. A month later he developed a fever, which was diagnosed as Malta fever, and on questioning him closely it was found that he had drunk the milk of a goat at Rosaires about sixty days before he fell ill. The fever was severe and he had successive attacks for nearly five months, but at the end of ten months he was considered well enough to return to duty in the Sudan. Being an intelligent observer he thereupon searched for the very goat whose milk he had habitually drunk the year before. He took a sample of the blood of this goat and sent it to England for examination. The blood was found to contain the microbe of Malta fever, proving that the goat was infected, and had, of course, been the cause of his fever.

So here at last was discovered a mode of infection which explains many of the curious features in the epidemiology of Malta fever, the irregular seasonal prevalence, occurring at one time and one place and at another time and another place.

It is most common in summer, rarer in winter months, when there are no mosquitoes and very little dust, and therefore it had been believed that the dust and the presence of the mosquitoes might be the cause, just as we believe that typhoid fever may get into the body by means of dust. But I do not propose to go through the various mistaken theories that had been propounded during past years; we now know that the infection is conveyed by the goat and through her milk. It is true that in Malta and most of the other places, which are all warm countries, there are more cases in summer, and this is partly explained by the temperature of the air being more favourable for the multiplication of the *Micrococcus melitensis*, and also by the fact that in the summer there is more cream used with fruit and for ice-creams, etc.

The fact of the existence of this poison in the milk explains now the curious fact that the officers, and even the officers' wives, suffered in a proportion which was about three times that of the men, that is to say, both soldiers and able-bodied seamen. The officer enjoys milk and cream in his tea and coffee, and the men do not. This fact also explains the isolated epidemics which have been from time to time reported. For instance, there was a case of a sergeants' mess, all the members of which were attacked by the disease, whereas the men living close by did not get it at all. That put out of court the possibility of the mosquito being the cause. The female mosquito (for it is the female only which bites) does not care whom she bites, and when a group of people are attacked and the remaining people outside are not attacked there may be something different in their food supply which accounts for it. In this case it was the fact that the sergeants at their mess had goats' milk, whereas the others had no milk at all.

When the milk discovery was made preventive measures in Malta were started as early as possible, in June, 1906. Of course the idea met with a certain amount of ridicule and prejudice and opposition, but by means of argument and persuasion the various regiments in Malta and the naval and military hospitals agreed to banish goats' milk from their dietary altogether.

At once there was a very striking result. For six years, taking the last quarter of the year only (because only that quarter is available for 1906), the average number of cases was 35·3 per thousand

of the strength. In the similar quarter of 1906, although that year began as badly as most other years, there were only 4·8 cases per thousand, that is to say, it was only about one seventh of the average which Malta had been accustomed to. In 1905 there were 643 cases, but in 1907 only 7 cases, and to-day there are none.

There are other striking instances: for example, the Royal Naval Hospital at Malta had a very bad reputation, so bad that the men of the Navy when they were sick preferred not to enter the hospital. When a man is very sick he is generally willing to leave his ship and go to a comfortable hospital on land to get well, but the naval authorities found that when a man was admitted for bronchitis or with a broken leg he contracted Malta fever in the hospital. But Malta fever has now been banished from the hospitals because goats' milk has been excluded from them, and since that change it is extremely satisfactory to note that not a single case of Malta fever has been contracted in them. If you add together the total number of days of sickness which the men of the army and navy suffered in the Mediterranean stations, you will find that in one year there were 70,000 to 80,000 days of illness due to this disease alone. If the absence of milk or the change of milk will succeed in stamping out this disease you will see at once that Malta, instead of being an unhealthy and dangerous station, will become a very healthy one, and we shall all agree that the Royal Society and the members of the Commission may be warmly congratulated on the successful issue of their investigation.

By the simple prohibition of the use of goats' milk, a prohibition due to experiments on a few goats and to those experiments alone, a serious disease has been exterminated. I think you will all agree that the end has justified the means, and that it was eminently worth while to shed the blood of those goats and other animals.

There is a curious anomaly connected with my own profession which I have never been able to understand; the general public talk of medical men as belonging to a "noble profession," they seem to find individual doctors humane, merciful, philanthropic, they accept without stint and without any visible bashfulness the help which is freely rendered them both at hospitals and in private life, they encourage the practitioner to lead an unselfish life by calling for his aid at all times, even when he is dining or sleeping. As a child cries for his mother the moment any pain or danger arises, so the people fly to a doctor for relief so soon as they make up their minds that their ill is beyond their own knowledge of domestic remedies. Yet when some people speak of physiologists and other workers who have elected to spend their lives in laboratories for the acquisition of knowledge which will benefit the world at large, instead of making money for themselves and their families by medical practice, they seem to be pictured as inhuman monsters of cruelty whose chief delight is the torturing of defenceless animals. Not being a physiologist myself I cannot pretend to know them all, but I have met many in my life in this country and have invariably been struck with their gentle kindliness to children and to animals.

The science which they teach is the science of life, from which is eliminated all sordid and selfish considerations. A scientist in his laboratory discovers a great truth, which saves the lives of thousands of human beings. The doctor engaged in everyday practice makes use of that knowledge perhaps to preserve the life of your child. Give him any praise you think fit, but don't entirely forget the physiologist who taught him the art. To understand the meaning of living processes it is necessary to study the living organism, and, in order to get knowledge, it is sometimes necessary to perform experiments on living animals. The law requires, and very properly requires, that these experiments can only be undertaken by properly qualified persons with a due sense of their great responsibilities. Due regard is paid to the comfort of the animals, and the ultimate aim of all experimental work is the acquisition of knowledge, from which ensues relief to suffering, which is so often only the result of ignorance.

Never forget that the benefits which result are felt not only by the human race but also by animals, for the veterinary surgeon gladly makes use of acquired knowledge in his daily practice. I have no desire to defend experiments which have not in view these great objects—growth of knowledge and relief of suffering. Neither do I attempt to defend any workers in any country who pay no consideration to the pain which an animal experiences.

So far as I know, the laws of this country are a

sufficient safeguard, but I think it is not sufficiently known to the public that physiologists obey the laws literally and are most punctilious in their observance. Professor Halliburton, who occupies the chair of physiology at King's College (London), in writing on this subject a few months ago, states that a certain number of trivial irregularities have been reported to the Home Office by the inspectors appointed under the Act of Parliament of 1876, called the "Act to amend the Law relating to Cruelty to Animals."

But the irregularities do not include any case of omitting to use anæsthetics to deaden pain. On the contrary, "the majority of these offences has been for using anæsthetics unnecessarily. A certificate in certain cases is granted for the omission of an anæsthetic: this is given when the operation is a trifling one, and has never been granted for any operation more serious than the prick of a hypodermic needle. Nevertheless the operator has sometimes employed an anæsthetic even for this, and has in consequence been reported to the Home Office for infringing the terms of his certificate."

Professor Pawloff, an eminent Russian physiologist, has very truly said that the ideal experiment is one which is performed without anæsthesia and without pain. In many cases this ideal can be realised, but sometimes it is impossible. In such cases physiologists have therefore had to decide which of the two disturbing factors shall be absent, and without hesitation they have decided that pain must be excluded. There are at least three reasons why physiologists, in case of need, prefer the use of anæsthetics to inflicting pain: (1) on the grounds of humanity, for I have already said that you have no right to assume that the man of science, unknown to you, is less humane than the average doctor with whom you are acquainted; (2) because pain disturbs the normal functions of an animal much more than anæsthesia or artificial sleep can do, and the experimenter of course wants the animal to be in as normal a state as possible; and (3) because when an animal is in pain or discomfort it naturally struggles, and this will not only prevent the accuracy of the experiment, but will endanger the safety of the delicate apparatus employed in the experiment. The most cruel, hard-hearted man, with absolutely no love for animals, would, therefore, for his own selfish protection, be obliged to send his animals to sleep before he attempted any delicate or prolonged experiment. Precisely the same arguments apply to the use of modern methods of surgery in those experiments where it is necessary to keep an animal alive after an operation in order to study the after-effects of the operation.

By modern methods I mean the use of antiseptics, which are chemical agents, to neutralise germs of impurity in and near the wound, or the aseptic method, which aims at the complete destruction of all such germs on the operator's hands, clothes, instruments, surgical appliances, bandages, as well as on the skin of the animal to be operated on. If such a method is employed the healing process is painless, fever and local inflammation are absent, and the wound will require dressing only once a week instead of twice a day as in the old-fashioned time. These daily manipulations used to prove much more distressing to the patient than the operation itself.

Thus it is for two reasons that an experimenter treats an animal with the same skill as he would a human being; to save the animal suffering and to insure the success of the experiment.

Another Royal Commission is now considering the whole question of experiments on animals, and if you have time to look through the four Blue-books of evidence which have been already printed you will see that the charges of cruelty have been patiently sifted one by one to the bottom, and in no single instance has an accusation of cruelty been sustained. But it is not only physiologists who are permitted by the State to experiment on animals in the United Kingdom. There are also pharmacologists and pathologists. The pharmacologist considers it his duty to investigate the action of new drugs upon animals before allowing the practitioner to experiment upon his human patients. You remember the old satire, which was certainly well deserved, before the days of experimental research: "The physician pours drugs, of which he knows little, into bodies of which he knows less."

The pharmacologist is able to carry on his experiments with drugs under anæsthesia the same way as the physiologist does. But the experimental work of the pathologist is different, for he conveys germs and other products of disease to animals. If a warm-blooded animal takes the disease suffering

is produced. That cannot be denied, and I have no doubt that the monkeys in Malta of whom I have spoken suffered somewhat when they became victims of a long, tiresome fever. The whole point is whether it was justifiable to make those monkeys suffer. We have no means of accurately measuring the amount of pain which the animals usually employed—rats, guinea-pigs, or rabbits—really feel when a disease is experimentally given to them; nor do we know if their pain is greater or less in amount than the suffering endured by such an animal when another disease or a violent death kills it in the usual course of Nature.

There is, however, one point on which we can be quite sure: the suffering of these animals is much less than that of human beings. Like any other animal a man who is ill suffers some discomfort and physical pain, but in addition he suffers much more from worry and anxiety about the present and the future. All this worry does not affect the sick rabbit. The pathologist is aware of the pain which he inflicts on the guinea-pig, but he looks beyond it to the pain which he hopes to prevent in human beings. For the death of a few small animals has already been the means of preventing pain and disease both to thousands of animals and millions of the human race.

There is one piece of evidence given before the Royal Commission which I wish to quote to you, because it was given by one of the keenest legal intellects of modern times, by Lord Justice Fletcher Moulton, who was senior wrangler and first Smith's prizeman of his year at Cambridge. He begins his evidence by taking the case of a ship infected with plague and infested also with rats, which are the carriers of plague from one country to another. Before the ship enters a port, say of Great Britain, is it better to kill the rats in order to prevent them and the disease from landing and causing an outbreak of plague in an innocent town, or is it preferable to refrain from doing so because the slaughter of the rats would be painful to them? The captain who orders the rats to be destroyed inflicts pain and death on them in order to prevent greater pain and more widespread death among human beings. If the captain, on the other hand, spares the rats, he is guilty of the criminal act of causing the death of many men, women, and children.

The opponents of all experiments on animals can only see the pain inflicted on dumb creatures; they seem unable to realise the pain prevented by the experiments. They have even been known to abuse Lord Lister, although he, more than any other man living, has been the means of preventing the greatest suffering and of checkmating for a time our common enemy, Death. They see very plainly the pain which he deliberately caused to a few rats and rabbits, but they seem incapable of understanding the incalculable amount of misery which he has prevented.

The Lord Justice also points out that the pain inflicted in all the laboratories of the United Kingdom during a year is quite infinitesimal compared with the pain inflicted every day in the slaughter of animals for food; in the operations performed without any anæsthetics by ignorant farm labourers in order that beef or mutton may be more tender or have a more pleasant flavour for the consumer; in sports, where birds and beasts die a lingering death, when they are maimed but not killed outright by sportsmen; and in fashion, which women thoughtlessly allow in order that their hats may be adorned with feathers and their bodies clothed with fur. All these methods of giving pain are permitted without protest, while "the one justifiable bit of pain in the whole world," which has for its object the prevention of future pain, is unhesitatingly denounced. Among the many striking examples of the benefits which experiments upon animals have conferred upon humanity I may mention two.

Cattle plague or rinderpest, which used to destroy hundreds of thousands of cattle every year in South Africa and other parts of the world, has now been prevented at the expense of a few animals —sacrificed by Professor Koch and others—and I read in the 'Times' of January 1st of this year that a Chicago firm has had to close its branch at Cape Town because South Africa can now supply itself with meat.

In India there are more than 20,000 deaths every year among our fellow subjects from the bites of poisonous snakes. Venomous snakes are found almost all over the temperate and tropical regions of the world, though in England and Europe generally it is only small vipers or adders which are found. Yet even in Europe snakes are dangerous to life, for out of 610 cases of viper-bite, 10 per cent., mostly in children, were fatal.

In Asia and Africa the cobra is the most poisonous snake, being armed with two poison-glands about the size of a large almond. Snake venom, when removed from the reptile and dried, can be kept for at least twenty years without losing its deadly power. The first symptom after a bite from a cobra is a sensation of burning pain at the place bitten, which soon becomes red, tender and swollen. After an interval of about half an hour the constitutional symptoms begin; the patient feels intoxicated, sleepy, weak in his legs and unable to stand. Running of saliva from the mouth, paralysis of the tongue and throat, with inability to speak or swallow, are followed by more general and decided evidence of paralysis. The patient lies on his back, incapable of movement, his breathing becomes slower, and the action of the heart quicker. At last the breathing ceases, with or without convulsions, and the heart stops beating. If the patient is fortunate enough to survive the severe paralytic symptoms he rapidly returns to his normal state of health.

The symptoms following the bite of the European viper are less severe, but within one to three hours after the bite great prostration sets in, accompanied by vomiting and often diarrhœa, with cold, clammy perspiration. The pulse becomes extremely feeble, and the patient, if a child, loses consciousness. In from twelve to twenty-four hours the severe constitutional symptoms usually pass off, leaving for a few more days great swelling and discolouration at the site of the bite.

Serum treatment of snake poisoning.—All the old-established methods of treatment, such as sucking the wound, have failed us, but recent research has shown that the true antidote for snake poisoning lies in the direction of serum treatment. From time immemorial the belief has been current, in many lands where poisonous serpents are common, that the repeated injection or eating of snake-poison could render an individual immune or snake-proof. It is undoubtedly true that some native snake-charmers have acquired a considerable amount of resistance to the poison in consequence of having been repeatedly bitten by snakes.

Immunity against one species of snake does not, however, protect the individual against other species. Dr. C. J. Martin tells the story of a European in Australia who used to handle the tiger-snakes with impunity, and was often bitten by them without real harm, yet he died on the day after he had been bitten by another poisonous species, the copper-head snake.

In 1894 Professor Calmette, of Lille, published to the world the news that an animal which has been treated repeatedly with the venom of a poisonous snake, such as the cobra, can yield a serum which is antitoxic to that poison. By subjecting horses to gradually increasing doses of snake-venom, and by patiently continuing the process for a year and a half, he succeeded in making the horses immune against the poison, and then by removing the serum he was able to furnish an antitoxin of practical value for use in India.

As in the case of the Australian I have just mentioned, the horse, being only protected against one species of snake, cannot give protection against other species, but an attempt is now being made in the direction of supplying one serum to act against two venoms, for from the Pasteur Institute at Kasauli in India there is now being issued a serum which is prepared by immunising horses with the poisons of the cobra and the daboia, which are the two snakes chiefly responsible for deaths in India.

I will not allude to diphtheria to-night, because I hope to devote to-morrow's lecture to it. But with regard to all these preventable diseases I would remind you that bacteriology is the foundation stone of public health. It is by hygienic precautions that certain diseases are prevented, and the basis of bacteriology is experiment on animals. But I should like to quote again from Professor Halliburton on the general questions of serum treatment, which has been stigmatised as "messy," besides some less elegant criticisms: "Filth or dirt," he says, "has been well defined as matter in the wrong place. Blood on a carpet, for example, is certainly messy and dirty; it ought not to be there. But blood or serum in the heart or in the arteries and veins is in its rightful place, and it does its duty of nutrition when it comes into more immediate contact with the tissues—the small tubes we call the capillaries. One of these duties is to exert a protective influence upon the whole body, by destroying the germs of disease which get into the body in spite of all precautions." I have pointed out to you in former lectures that we are all of us exposed, so long as spitting in public places is not prohibited, to the germs of consumption, yet few of us catch that disease. This is because the white corpuscles of our blood are in good order and are able successfully to devour the bacteria that enter our bodies. It is those people who are run down and in whom the white corpuscles are not active who catch this disease. In assisting the white corpuscles to perform this most important

function, the co-operation of certain substances dissolved in the fluid portion of the blood is also necessary. The most recently discovered of these auxiliary substances have been called opsonins by Sir Almroth Wright. The word "opsonin" is derived from a Greek root which means "to prepare the feast." The opsonin either adds something to the germ which makes it tasty to the white corpuscle or removes something which previously made it distasteful. This is not mere fancy; the whole sequence of events can be followed on a glass slide, kept at the temperature of the body and examined under a microscope: "If the yeast plant (which is similar in many ways to bacteria) is grown in a solution of sugar, the sugar is broken up and disappears, and two new substances formed from the sugar take its place. These two substances are alcohol and carbonic acid gas. If bacteria grow in the blood they do not produce alcohol, but they do produce other poisons in an analogous way. These poisons are called *toxins*. There are substances in the fluid part of the blood which are called *antitoxins* because they neutralise the toxins produced by the bacteria. Their presence constitutes a means of defence against the harmful effects the toxins would otherwise produce. The marvellous part of the defence is that, although we all have a certain amount of antitoxin in our blood, the amount increases in proportion to the amount of toxin. The presence of a toxin stimulates the living cells to produce more and more antitoxin, and the blood remains rich in the antitoxin for a considerable time afterwards." Now you understand why a person who has had an infectious disease does not readily catch it again; he is immune to that special disease for some years because his blood is so rich in the antidote. This is true for most of the ordinary infectious diseases, but is often not true for influenza. I have, I hope, said enough on this subject to make you believe that by recently invented serum treatment we are helping Nature and not going against her. Nature uses serum for curing infectious diseases, and the introduction of an opsonin or an antitoxin is not putting matter into its wrong place but into its right place.

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June 7th, 1909.

DIAGNOSIS OF MALIGNANT DISEASE BY ESTIMATING THE ANTITRYPTIC POWER OF CANCEROUS SERUMS.

By E. C. HORT, B.Sc., M.R.C.P.Ed.

MANY attempts have been made in recent years* to measure the differential variation in the antitryptic values of normal and pathological serums. Of these the latest and most successful is that introduced by Dr. Golla,† who has shown that by using the physical method of electro-conductivity of Henri the antitryptic power of tuberculous serums can be accurately gauged.

The object of this note is to show that by using A. R. Smith's‡ adaptation of Sörensen's§ method of measuring the amino-acid production in a tryptic digestion it is also possible correctly to estimate the relative antitryptic power of serum in health and disease by chemical means.

So much, in fact, is this the case that, as I shall show, a series of cases of malignant disease of various organs exhibited such marked variation from the normal in the antitryptic value of their respective serums when examined in this way as to justify the hope that the method will prove to be of great clinical value in the diagnosis of doubtful cases of cancer.

The test is a very simple one, and requires only the power of accurate volumetric and gravimetric determination. I have submitted it to the most rigid trials and find that two observers working in two laboratories and using different stock solutions can, when measuring the same serums, produce identical results within a limit of experimental error of less than 5 per cent.

The *modus operandi* is briefly as follows, four solutions being required:

* *v.* CLINICAL JOURNAL, April, 1909, "The Antitryptic Index."

† Golla, 'Lancet,' March, 1909.

‡ A. R. Smith, 'Biochem. Journ.,' June, 1909.

§ Sörensen, 'Etudes enzymatiques, Lab. de Carlsberg,' 1907, 7, 1. As is well known, if a solution of formaldehyde containing a trace of phenophthalein be added to a solution of casein, or other proteid submitted to the action of trypsin, the concentration of carboxyl groups liberated can be estimated by titration. This method of determining the velocity of enzymic activity is based on Schiff's discovery of the action of formaldehyde in neutralising and converting the NH_2 groups into NCH_2 (*v.* Bayliss, 'The Nature of Enzyme Action,' 1908, p. 24).

Solution A: 4 per cent. solution casein.

Solution B: ·5 solution trypsin.

Solution C: NaOH N/5.

Solution D: (1) alcoholic solution phenophthalein; (2) formaldehyde; when required for use add 1 c.c. (1) to 50 c.c. (2).

Method.—To one flask containing 25 c.c. of A add 20 c.c. dist. water in the cold. To a second add ·5 c.c. dist. water to 5 c.c. of B; heat both flasks for thirty minutes at 38° C. Then mix contents of flasks and incubate at 38° C. for 4½ hours, which time numerous experiments show to give the maximum variation when the serums are added. Ten c.c. are then withdrawn and 5 c.c. of solution D added, which has been neutralised with NaOH N/5 till faintly rose-coloured, and that quantity immediately titrated. This neutralisation must be performed immediately before using D, as the formaldehyde readily oxidises and free formic acid appears. The amount of NaOH N/5 required to produce the standard shade of colour fixed on is read off. An equivalent quantity of the digest is titrated before digestion takes place, and the difference in the amount of alkali used is considered to be the equivalent of the carboxyl acids formed by the action of the formalin on the amido-acids liberated by digestion. In order to measure the inhibitory power of the serums to be examined it is only necessary to repeat the experiment, substituting ·5 c.c. of serum for ·5 c.c. of dist. water.

Example 1.

Ten c.c. of digest containing no serum required after 4½ hours' digestion 1·8 c.c. of NaOH N/5 to effect neutralisation after making the necessary correction.

Ten c.c. of digest containing ·5 c.c. of normal human serum required after 4½ hours' digestion ·70 c.c. of NaOH N/5 to effect neutralisation after making the necessary correction.

Ten c.c. of digest containing ·5 c.c. of cancerous serum required after 4½ hours' digestion ·45 c.c. of NaOH N/5 to effect neutralisation after making the necessary correction.

Example 2.

Ten c.c. of digest containing ·50 c.c. of normal horse-serum required after 3 hours' digestion 1·20 c.c. of NaOH N/5.

Ten c.c. of digest containing ·75 c.c. of normal horse-serum required after 3 hours' digestion 1 c.c. of NaOH N/5.

Ten c.c. of digest containing 1 c.c. of normal horse-serum required after 3 hours' digestion ·70 c.c. of NaOH N/5.

I found it impossible to use normal horse-serum as a standard, as different samples bear no constant relation to normal human serum. The antitryptic content of serum from different horses, presumably healthy, shows, in fact, great variation when estimated by this chemical method—a point of considerable importance to remember in connection with its internal administration.

In order to determine the constancy of the antitryptic value of different samples of normal human serum the blood of thirty individuals has been examined. Of these ten were healthy adults, the remaining twenty being cases of hernia, acne, furunculosis, hydrocele, floating kidney, chronic gastric ulcer, varicose ulcer, and other conditions in which there was no evidence of a general infection. In all thirty cases the antitryptic value of the serum was lower than in any of the cases of malignant disease except one, which is referred to later. The constancy of the antitryptic content of normal human serum can be appreciated from the following experiment, in which six serums from presumably healthy adults were examined with the same solution and on the same day.

Experiment.

Ten c.c. of digest containing no serum required 1·80 c.c. of NaOH N/5 to effect neutralisation, whilst:

Ten c.c. of digest containing ·5 c.c. of serum from healthy subject 1 required ·70 c.c. of NaOH N/5.

,,	,,	2	,,	·70	,,	,, ,,
,,	,,	3	,,	·70	,,	,, ,,
,,	,,	4	,,	·70	,,	,, ,,
,,	,,	5	,,	·68	,,	,, ,,
,,	,,	6	,,	·68	,,	,, ,,

With a different solution on a different day—

Ten c.c. of digest containing no serum required 1·80 c.c. of NaOH N/5 to effect neutralisation; whilst—

Ten c.c. of digest containing ·5 c.c. of serum from patient with abdominal pain required	·58	NaOH N/5	
patient with hæmorrhoids	,,	·60	,, ,,
healthy adult . . .	,,	·60	,, ,,
healthy adult . . .	,,	·61	,, ,,

Variation in the antitryptic value of normal human serum at different hours of the day and before and after food, and on starvation, has been shown by Dr. Golla to be negligible when measured by the method of electro-conductivity, so the observations have not been repeated with the chemical method.

In order to ascertain in what proportion of cases of malignant disease the antitryptic content of the blood undergoes variation the serums of thirty-five consecutive cases were examined. In thirty-four of these the antitryptic content was markedly raised; in the last a normal content was found. The case with normal content was one of duct-cancer of the breast, confirmed by microscopical section, in a lady, æt. 83 years, with no enlargement of axillary glands and entire absence of cachexia. In all of the thirty-four cases in which the blood examination was in favour of a positive diagnosis of malignant disease the clinical evidence of malignancy would seem to be indisputable.

Experiment to Show the Relation of the Antitryptic Value of Serum from Six Cases of Malignant Disease to that of Normal Serum.

Ten c.c. of digest containing ·5 c.c. of normal serum required 1·20 of NaOH N/5 after five hours' digestion, whilst—

Cancerous serum	1	required	·80	of	NaOH	N/5
,, ,,	2	,,	·78	,,	,,	
,, ,,	3	,,	·86	,,	,,	
,, ,,	4	,,	·92	,,	,,	
,, ,,	5	,,	·80	,,	,,	
,, ,,	6	,,	·94	,,	,,	

Table of Thirty-two Cases in which a Positive Diagnosis of Malignant Disease based on a Rise in Antitryptic Power Confirmed the Clinical Diagnosis.

1.	Camberwell Infirmary	Carc. cervix	·35	·65
2.	,, ,,	Carc. breast	·51	·65
3.	,, ,,	Carc. rectum	·45	·65
4.	,, ,,	,, ,,	·35	·65
5.	,, ,,	,, ,,	·45	·65
6.	,, ,,	Carc. œsophagus	·54	·70
7.	,, ,,	Carc. breast	·49	·70
8.	,, ,,	Carc. colon	·56	·70
9.	,, ,,	Carc. tongue	·70	·96
10.	,, ,,	Carc. mesentery	·84	·96
11.	,, ,,	Carc. cervix	·85	·95
12.	,, ,,	Carc. rectum	·77	·96
13.	,, ,,	Carc. stomach	·80	·96
14.	Camberwell Infirmary	Carc. intestine	·76	·96
15.	,, ,,	,, ,,	·76	·96
16.	,, ,,	Carc. larynx	·68	·96
17.	Middlesex Hospital	Carc. tongue	·50	·60
18.	,, ,,	Carc. rectum	·50	·60
19.	,, ,,	Carc. palate	·52	·60
20.	,, ,,	Carc. cerv. glands	·62	·82
21.	Cancer Hospital	Carc. sigmoid	·45	·60
22.	,, ,,	Carc. scrotum	·40	·60
23.	,, ,,	Carc. mouth	·45	·60
24.	St. George's Hospital	Carc. breast	·45	·60
25.	,, ,,	Carc. cervix	·75	·80
26.	Private	Carc. breast	·43	·56
27.	,,	Carc. cervix	·41	·56
28.	,,	Carc. mouth	·85	1·00
29.	,,	Carc. cervix	·90	1·00
30.	,,	Carc. breast	·76	·96
31.	,,	Carc. tongue	·90	1·05
32.	,,	Carc. cæcum	·95	1·05
33.	,,	Carc. abdomen	·68	·80
34.	,,	Carc. breast	·72	·90
35.	,,	,, ,,	Normal.	

In each case the first figure represents the amount of NaOH N/5 required to neutralise the cancerous serum, the second figure representing the amount required to neutralise the normal serum.

Appended are notes of five cases to show the value, from a clinical standpoint, of measuring the antitryptic power of cases suspected to be cancerous.

Case 1 from a lady, æt. 45 years, with a mammary tumour, suspected to be a malignant adenoma. Ten c.c. of blood were withdrawn from the median cephalic vein. The amount of NaOH N/5 required to neutralise 10 c.c. of digest containing ·5 c.c. of her serum was ·65 c.c., whilst the amount required to neutralise 10 c.c. of digest containing ·5 c.c. of serum from a healthy adult was ·90 c.c. A positive diagnosis was therefore made and the breast removed. The diagnosis was fully confirmed by microscopical section.

Case 2.—A gentleman, æt. 63 years, consulted me for rapid loss of weight, vomiting, and severe epigastric pain and tenderness. The stomach was dilated and a sense of resistance in the pyloric area was undoubted. A provisional diagnosis of malignant disease in the neighbourhood of the pylorus was made and exploration advised. The patient was then seen by two surgeons, who independently gave a similar diagnosis and similar advice. The blood examination, however, showed that the antitryptic power of the patient's serum was normal, that is, the amount of NaOH N/5

required to neutralise 10 c.c. of digest containing ·5 c.c. of the patient's serum was the same as that required to neutralise 10 c.c. of digest containing ·5 c.c. of serum from a known healthy subject, viz. ·80 c.c. Operation was performed, and the only lesion found was a band of old adhesions between the gall-bladder and the stomach. This was divided and the patient is now in perfect health.

CASE 3.—A man, æt. 52 years, was sent for examination on account of suspected malignant disease of the rectum. No lesion could be discovered on examination *per rectum*, the only point in favour of the diagnosis being slight hæmorrhage from the bowel. Clinically the diagnosis could not be supported. Examination of the blood showed a normal antitryptic content.

CASE 4.—The blood of a woman in whom malignant disease of the cervix had been suspected clinically was found to have a high antitryptic content; subsequent operation and microscopical section revealed the correctness of both clinical and hæmatological diagnosis.

CASE 5.—A lady with signs of intestinal obstruction was found to have a high antitryptic power, the figures being ·60 and ·78 (normal). Operation revealed an inoperable mass of carcinoma with extensive lymphatic involvement.

I wish to make it clear that whilst convinced of the value of a normal antitryptic content in excluding malignant disease, a raised content does not necessarily support a positive diagnosis, since variation may occur in many other diseases. I find, for instance, that variation occurs in scarlatina, measles, acute appendicitis, enteric, leprosy, syphilis, and even in certain cases of fracture of long bones. Taken in conjunction, however, with clinical evidence, a high antitryptic value appears to be often of the greatest importance in the direction of a positive diagnosis of the presence of malignant disease.

I am deeply indebted to Mr. Pearce Gould at the Middlesex Hospital, to Dr. Lazarus Barlow in the Cancer Department, to Mr. Leaf at the Cancer Hospital, to Dr. Bayly at St. George's Hospital, to Dr. Keats at the Camberwell Infirmary, and to Mr. Cheatle and Dr. Gompertz at King's College Hospital for their courtesy in providing the necessary material for this investigation.

June 7th, 1909.

Gastric Erosions.—Berger draws the picture of this affection from nineteen articles in the literature. Pain in the stomach, weakness, and emaciation are the principal disturbances accompanying the erosions in the stomach, but the pain is never boring or cramp-like, as with gastric ulcer, and it seems to extend throughout the whole stomach, and is not affected by pressure or change of position. The pain comes on at once after eating, persists for an hour or two, and then gradually subsides, but it may persist all the time in some cases, irrespective of the intake of food. There may be intervals free from pain, during which the patient feels quite well, and the pains generally vanish after lavage of the stomach. Frequently there is no appetite, and there is often lassitude after eating, gradually subsiding in an hour or two. Pariser advises control investigation of the fasting stomach to differentiate erosions from gastric ulcer or a neurosis; it is especially instructive when burning pain throughout the entire stomach, in connection with the meals, is observed with emaciation, especially when the test breakfast has shown normal or subnormal acidity with or without excess of mucus. The course is protracted, with a great tendency to recurrence, and there is always danger of hæmorrhage from erosion of some blood-vessel. Treatment should be both local and general: lavage of the stomach with a 1 or 2 per 1000 solution of silver nitrate, large doses of bismuth, and the Lenhartz ulcer diet. He calls this form "Einhorn's disease." Quite opposite is the picture of simple ulceration of the stomach. It comes on abruptly, the first symptom being a serious hæmorrhage in the midst of health. The lesion is superficial, but it extends over a broader area than mere erosions. In the intervals between the hæmorrhages the patients feel well, with unimpaired appetite, and the stomach is not spontaneously painful or tender on pressure. Some advocate surgical treatment, but in certain cases that came to autopsy no eroded vessel could be discovered, showing that operative treatment would have had little chance of success. For this condition, also, treatment with the Lenhartz ulcer diet offers the best prospects, accompanied by bismuth, iron, and arsenic. This seems to be the only means of controlling this surface bleeding, strengthening the patient, and correcting the anæmia.—*Journ. A. M. A.*, vol. lii, No. 20.

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WITH MR. BLAND-SUTTON AT MIDDLESEX HOSPITAL.

IX.

On a Comparison of Cancer of the Lips and Cancer of the Labia.

Throughout this course of lectures I have taken every opportunity to emphasise the fact that cancer is more liable to attack an organ which is the seat of chronic disease than one which is apparently healthy. This also applies to the situations in which cancer arises on cutaneous and mucous surfaces, and accounts for the occurrence of carcinoma at the edges of chronic ulcers, whether on the skin of the leg or on the mucous membrane of the stomach, the margin of ulcers due to burns and scalds, X-ray burns, lupus patches and the like. Cases have been reported in which squamous-celled cancer has arisen in the scars left on the conjunctiva as the result of lime burns.

In this lecture I shall endeavour to show that primary cancer of the lips and of the labia support this contention in no uncertain way.

Cancer of the lip is a common disease; you will frequently see examples of it in the out-patient room and in the wards. In these departments you will see this disease in the early and operable stages, but in the inoperable and advanced conditions you will also have opportunities of studying it in the cancer asylum connected with this hospital. I shall assume for the purposes of this lecture that you are familiar with the clinical features of cancer of the lips and of the labia. In its age-incidence it shows nothing uncommon in comparison with cancer in other regions of the body. Mr. C. W. Rowntree, in a careful statistical study of cancer of the lips contained in the 'Archives of the Middlesex Hospital,' 1906, vol. vii, p. 118, calculated the age-incidence as ascertained from 202 patients to be 56·4 years. He points out that the youngest

age at which this disease has been reported, and on the strength of a microscopical examination, is the thirteenth year (Johnstone and Batashoff). A case has been reported in a man of the great age of 103; this patient was submitted to operation by Jalland in 1891.

This disease in the lips does not differ from cancer in other regions of the body in the relentless way in which it destroys the tissues according to the lip affected, and the manner in which it infects the lymph-glands in the submaxilliary triangles and the submental space: the gradual fusion of the cancerous lymph-glands followed by the implication and ulceration of the overlying skin, and the formation of a huge cancerous ulcer in the neck, on the floor of which the carotid vessels may be seen pulsating; and in due course the ulceration may breach their walls and lead to fatal hæmorrhage, unless the patient dies earlier from exhaustion produced by repeated small losses of blood, or septic infection of the lungs, due to the inhalation of foul material incident to the septic infection and sloughing of the cancerous tissues.

Cancer of the lip has a great interest for those who are investigating the cause of cancerous diseases, on account of the greater frequency with which it arises in the lips in men as compared with women, and the greater liability of the lower as compared with the upper lip.

In this hospital during the years 1897–1907 (both inclusive) there were fifty cases of carcinoma of the lips admitted into the surgical wards, the greatest number admitted during one year being seven and the least one. Of these fifty patients all were men. In two men the site of the growth was the upper lip; in the remainder the lower lip was affected, but in three of these forty-eight patients the cancerous ulcer began at the angle of the mouth.

This preference of cancer for the lower lip is shown in a striking way by the cases tabulated by Loos in Brun's Klinik at Tubingen. Out of a total of 565 patients 534 arose in the lower lip, and of these 467 were men and 67 women. It is also remarkable that though men are infinitely more liable to cancer of the lower lip than women, yet the liability is equal for both sexes in regard to the upper lip. In the 565 cases collected by Loos 31 occurred in the upper lip, and of these 16 were men and 15 women. In regard to the lower lip it may be stated that the disease rarely begins in the middle line, and the liability of the right and left halves is practically the same.

The figures given above indicate that men are much more liable to suffer from cancer in the lower lip than women; and that cancer of the upper lip is an uncommon disease, and that the cases are fairly equally distributed between men and women.

The increased liability of men to cancer of the lip as compared with women is attributed to the greater frequency of tobacco smoking among men as compared with women. In connection with this matter it may be mentioned that cancer of the lip is sometimes spoken of as "countryman's cancer," on account of the frequency with which it occurs among agricultural labourers who use short-stemmed dirty pipes. The clay pipes with short stems are very convenient as they can be carried in the pocket. In this hospital some of the patients come under the heading "farm-labourers," but many are men who come under the term "labourers," and their custom in regard to the short pipe is the same as the farm-hand. The stem of such a short pipe soon becomes hot when in use and burns or scorches the lip.

Women, too, who work in the fields acquire the habit of smoking short clay pipes, and, as far as my observations go, in Germany more women work in the fields than is the custom in England. This may account for the greater prevalence of cancer in the lip in women as shown in the tables prepared by Loos, than we find from an analysis of the list from our own hospital.

It is possible that chronic syphilitic ulcers of the lips may become cancerous and account for a certain number of cases which occur in non-smokers. This is undeniably true of the tongue. It is also certain that cancer is occasionally seen in the lips of patients who do not smoke tobacco and who are not tainted with syphilis. It is also worth bearing in mind that cancer of the lip is a common disease among those whom we regard as the "working-class," but this set of men and women does not by any means monopolise tobacco. Many professional men, including the vicar of the parish, smoke as hard as the labourer, yet it is excessively rare to find a case of cancer either of the upper or lower lip among them.

The preference of cancer for the lower lip is not easily explained. The distribution of malignant ulcerations of the face is an enigma. How rare it

is to find squamous-celled carcinoma attacking any part of the cutaneous covering of the face save the lips, and why should rodent ulcer grow in the skin of the eyelids, the margin of the nasal orifices, and on the cheek, yet be unknown on the chin and lips?

Let me now take you to another part of the body, namely, the labia, where the anatomy is similar to that of the lips, and let us study it in relation to trauma and carcinoma.

The labia majora are two large parallel folds of skin extending from the mons veneris to near the anus; they form the boundaries of the rima pudendi.

The cutaneous outer surfaces of the labia are beset with hairs and sebaceous glands, and the skin is more deeply pigmented in this part than in other regions of the body. The opposed surfaces of the labia are pink, and possess rudimentary hairs and very large sebaceous glands.

The labia minora are two pink cutaneous folds lying parallel with the greater labia. They are hairless, but rich in large sebaceous glands. Anteriorly they become confluent at the frænum of the clitoris, but posteriorly they are gradually lost on the inner surfaces of the labia majora.

There are some points connected with the age-changes of the labia which need consideration. During infancy the greater labia appear as two parallel cutaneous eminences, and the thin edges of the smaller labia project between them and are pink, like mucous membrane. At puberty the hair becomes conspicuous on the outer surface of the labia majora, and these cutaneous folds increase in size and usually conceal the labia minora. Their opposed or inner surfaces remain pink, whilst the outer surfaces become pigmented, especially in brunettes. In many women the labia minora remain concealed by the labia majora, but in others they grow unduly and protrude beyond the vulvar cleft and resemble a pair of molluscan palps. They then undergo a curious change, for those parts covered by the greater labia retain their pinkness, and possess as usual very large sebaceous glands, but the palp-like portions become deeply pigmented and lose their sebaceous glands; occasionally delicate hairs, two or more centimetres in length, grow from them. Labia majora elongated in this way are sometimes termed "hypertrophied nymphæ," a condition which reaches its maximum in Hottentot women, whose "apron" is formed of greatly elongated nymphæ (Fig. 1).

After the forty-fifth year the hair on the mons veneris and labia, like that on the rest of the body, tends to lose its colour, becomes white, and is gradually shed; the greater labia shrink as the fat disappears, which causes the nymphæ to be exposed and the vulvar orifice becomes narrowed. Occasionally this shrinking of the parts is excessive, and the labia, big and little, become markedly atrophied, so that the inner surfaces of the labia are exposed; they become smooth and shiny, with here and there red patches which are exquisitely tender. Coincident with such extreme changes the vaginal orifice is narrowed, and in some instances will

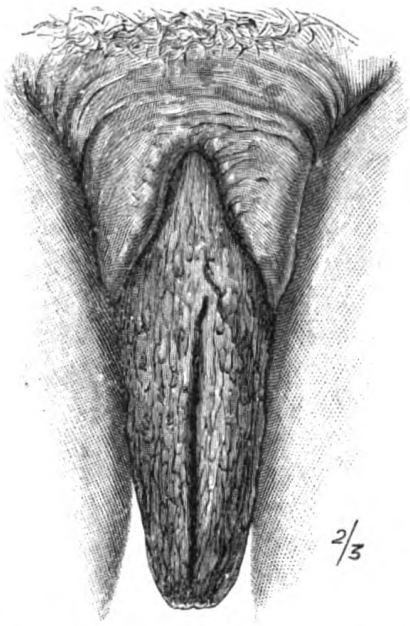

FIG. 1.—The Hottentot "apron." It is formed of the greatly elongated labia minora. (After Blanchard and Lesueur.)

scarcely admit a finger. The hairs on the labia and mons are scanty, coarse, and broken; finally the labia become almost as colourless as skin, and all the folds and creases look as if they had been smoothed out.

In such extreme cases the patients complain of great irritation, excessive pain during sexual intercourse and micturition. For this condition the name "kraurosis" (χραῦρος, dry, withered) is applied, and it is very troublesome and inconvenient in married women, but spinsters rarely complain of it.

No particular cause is known to account for this condition, and it is frequently associated with atrophy of the uterus, and is occasionally seen as a

sequel to bilateral ovariotomy, oöphorectomy, and hysterectomy.

Kraurosis is a condition of interest to us, for it may be regarded as a pre-cancerous condition, but before considering this matter I wish to draw your attention to another change to which the vulvar epithelium is prone, and which is also a precancerous condition.

It is well known that the mucous membrane of the tongue in middle-aged men, especially of those who smoke and of those who are syphilitic, often presents irregular white patches, a condition known as "leukoplakia." These white patches are due to thickening of the epithelium and small-celled infiltration of the subepithelial layer. Sometimes these patches are so thick that the affected area of the tongue looks as if coated with white paint. This leukoplakic condition of the lingual mucous membrane is of sinister significance, because clinical observation has shown that squamous-celled cancer is very liable to arise at the edges of such patches, or in the deep fissures which sometimes traverse them.

In 1895, when I became surgeon to the Chelsea Hospital for Women and thus had excellent opportunities for observing diseases of the vulva, I noticed in many of the patients who came complaining of vulval irritation that some of the cases, which would be classed on cursory examination as examples of kraurosis, presented appearances which, had they been situated on the lingual or buccal mucous membrane, would be called leukoplakia. Subsequently I satisfied myself that this condition is identical with lingual leukoplakia, and like it is often the forerunner of squamous-celled cancer.

I drew attention to the matter in a book which I published on 'Diseases of Women' with the assistance of Dr. A. E. Giles in 1897 (p. 86). Since that date other surgeons have published reports of cases of cancer of the vulva showing the close association of the two conditions. In my early observations I held the opinion that in all probability syphilis was the cause of vulvar leukoplakia, but more extensive observations have convinced me that it occurs independently of this disease. It is worth mention that Bonney has made a careful histological investigation of vulvar leukoplakia, which shows that the changes in the epithelial and subepithelial tissues are identical with those produced by this pathological condition in the tongue ('Archives of the Middlesex Hospital,' vol xiii, Seventh Report from the Clinical Research Laboratories).

Carcinoma of the vulva.—In discussing cancer of the lip I mentioned to you that in the years 1897–1907, both years inclusive, fifty cases of cancer of the lip (all men) were admitted into the surgical ward of this hospital. Dr. Comyns Berkeley informs me that in the decade 1898–1908 there were fifty-seven women admitted into this hospital and the Chelsea Hospital for Women with carcinoma of the vulva, and that in all the patients the inner surfaces of the labia majora presented the condition known as kraurosis, or leukoplakia. When the social histories of these women are analysed they are instructive, because among these fifty-seven patients there were fifteen widows, thirty-four married women, and eight spinsters. These observations indicate that the trauma connected with coition and childbirth are probably factors in producing the changes which render the epithelial tissues of the vulva liable to cancer. I have satisfied myself that some of the patients were syphilitic.

It is a significant feature in relation to vulval cancer that trauma connected with the sexual act and its results plays the same part in connection with the labia that the habit of smoking short, dirty, clay pipes exercises on the mucous membrane of the lips.

Cancer of the labia has many features in common with cancer of the lip. For example, it may arise in any part of the internal surface of a labium and destroy it, implicate the underlying tissues, and quickly infect the inguinal lymph-glands of the corresponding side. In some cases it arises in the angle between the greater and the lesser labium, near the anterior part, and then extends into the tissues which form the cutaneous hood of the clitoris and implicates the labium of the opposite side, in the same manner that cancer arising in the lower lip, near the angle of the mouth, will creep around the commissure and involve the upper lip, but there is this difference in the case of the labia: when the carcinoma spreads across the median fold into the opposite labium, the lymph-glands in both groins will become cancerous. It occasionally happens that cancer arises in the cutaneous hood of the clitoris, and in such circumstances it may be, and is sometimes, mistaken for carcinoma of the clitoris. It is essential to look carefully

into the precise relations of the cancerous ulcer to the labia, and it is worth while to note carefully when there is a large cancerous ulcer on one labium and another ulcer at a corresponding spot on the opposite labium, to determine, if possible, whether the two are connected by a band of cancerous infiltration either over the clitoris or across the vestibule, for it is maintained by some surgeons that when two cancerous ulcers exist in corresponding spots on opposed surfaces of the greater labia, that, in some instances at least, one of the ulcers is due to infection from the contact of a healthy labium with a cancerous ulcer on its fellow. Reputed instances of this are numerous, but when the facts are submitted to a critical inquiry few stand the test.

Cancer of the labium has an age-incidence which corresponds fairly with that for the lip, and it is probable that this disease is as common in women as is cancer of the lip in men. The disease runs a similar course, and as it involves the urinary meatus, and sometimes the anus, it leads to great distress in its late stages, and reduces its victims to a miserable condition.

From an operative point of view the results of the free and wide removal of the infected parts give excellent results if seen early. The wounds made by the operation heal quickly, and I find it a great advantage to remove the primary disease at the first operation, and fourteen days later when the parts are healed to thoroughly extirpate the lymph-glands in both groins. In removing the labia the surgeon takes care not to damage the urinary meatus. The precise method of dealing with the tissues surrounding this orifice varies according to the extent of the operation, but it is a matter which rarely causes difficulty. The complete extirpation of the lymph-glands in the groin in these circumstances is in keeping with the surgical measures employed against cancer of the lips.

It appears to me clear from a consideration, as well as a comparison, of the conditions surrounding cancer of the lips and of the vulva, that trauma plays a significant part in rendering the epithelium investing the lips and labia vulnerable to the parasite of cancer, inasmuch as frequently repeated injuries maintain the parts in a condition of chronic inflammation.

June 14th, 1909.

A CLINICAL LECTURE

ON

HEMIPLEGIA.

Delivered at St. Bartholomew's Hospital.

By SAMUEL WEST, M.D., F.R.C.P.,
Physician to the Hospital.

GENTLEMEN,—I find there is a good deal of confusion in the minds of students and candidates for examination on the question of hemiplegia. It is really an extremely simple affair; the confusion depends largely upon an incomplete grasp of the anatomical and physiological principles upon which the diagnosis depends.

Hemiplegia is a purely motor affection. I do not say there are not slight defects of sensation, and of other things too, but it is as purely a motor affection as anything you are likely to meet with in the nervous system. It consists of paralysis, complete or partial—generally complete—of one side of the body, arm, leg, and face. We have to consider, then, where the lesion can be that could produce a paralysis of motion only involving the whole of one half of the body.

The first physiological fact is that all these gross movements, like the movements of the arm and leg, are controlled from centres on the cortex of the brain. So that what we want to know first is something about the localisation of motor functions in the brain. And that is very simple. All the gross movements of the opposite half of the body are ranged in the parietal region round about the fissure of Rolando, leg, arm, hand, and face from above downwards. One other fact may be added, and that is that in the inferior frontal convolution, in the posterior part of it, on the left side—Broca's convolution as it is called—is located the motor centre for speech, and injury to this will prevent the patient from performing the complicated movements required for speech. If there be a lesion on the cortex of the brain which is to paralyse the leg and foot and hand and face, it must be very extensive and involve the whole of this motor area. We will come back to that directly (Fig. 1).

These motor centres in the brain are connected with the appropriate centres in the cord by bands of fibres; and the next thing we want to know is the

course these fibres run. From the motor cells in the cortex, the fibres run through the white central substance of the brain, the crus of which they form the chief part, and thence through the pons to the medulla. At the anterior pyramids the motor fibres cross and pass down the lateral columns on the opposite side, except one small bundle, which runs in the anterior columns on the same side. These are called the "crossed" and "direct" pyramidal tracts respectively. The fibres to the face muscles cross a little higher up, and those to the eye muscles higher still (Fig. 2).

paralysis of the third nerve on one side and paralysis of the muscles of the face and extremities on the other, we know that we have another form of crossed paralysis, dependent upon a lesion somewhere in the crus.

So far we have not yet got to the common form of hemiplegia at all. Therefore we may conclude that the lesion of the ordinary form of hemiplegia, where the paralysis affects the whole of one side of the body, must at any rate be above the crus and on the opposite side. We now want to know a little more about the course of the motor fibres

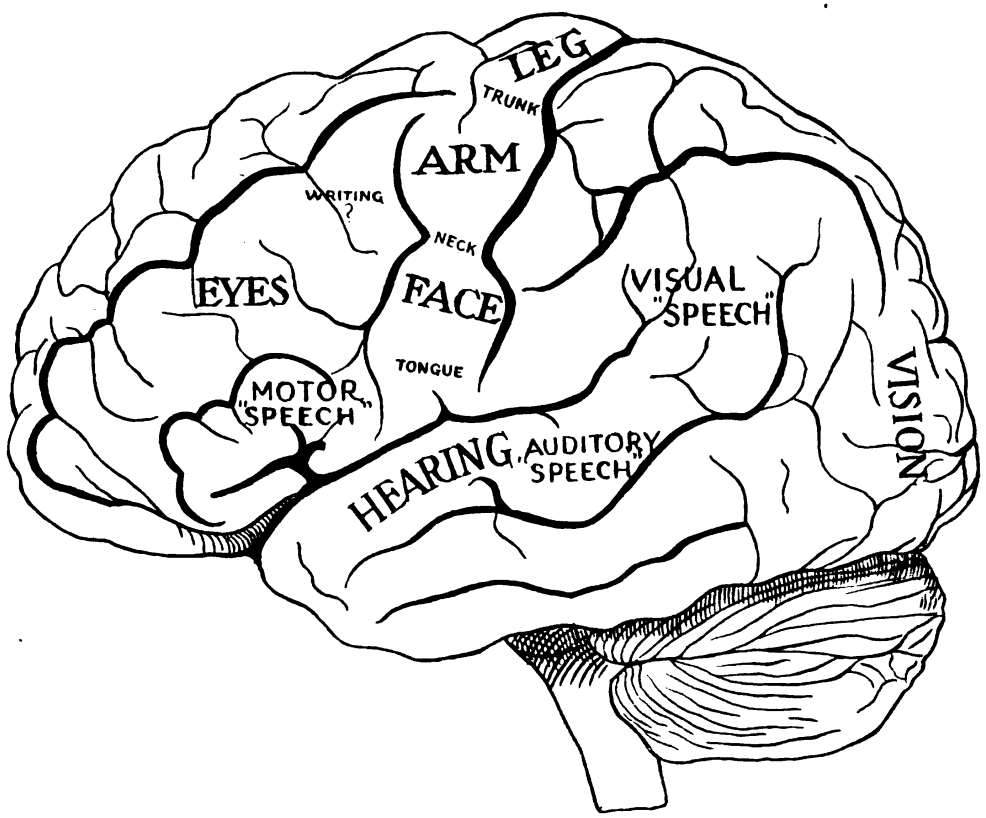

FIG. 1.—Centres on cortex

Now let us see how far we have got. If hemiplegia is to be produced the lesion cannot be below the decussation. Just above the decussation the muscles affected will be on the opposite side of the body as regards the leg and arm, but on the same side as regards the face. This is called *crossed hemiplegia*. The seat of the lesion, therefore, for crossed paralysis will be in the pons—that is to say, somewhere between the crossing of the facial nerve-fibres and the crossing of the fibres for the lower limbs. A little higher up, above the facial nerve centre, the muscles for the eye cross, so if there be between the crus and the cortex. You can imagine the fibres coming from the surface of the brain from all sides in the shape of a curved or warped fan: the crus is the handle, and just before the crus, formed by the rays of the fan while they are still somewhat spread out, is the internal capsule. This is thin looked at sideways, and broad if looked at from above or below. That is an important fact to remember, because if the internal capsule is so thin a lesion which involves the internal capsule only would have to be a very small lesion.

Let us now take another section of the brain

which shows the great ganglia at the base of the brain. In front is the caudate nucleus, below and outside is the lenticular nucleus or striate body, and still lower and behind is the optic thalamus. Surrounding the lenticular nucleus and lying between the caudate nucleus in front and the optic thalamus behind is the internal capsule, of which two thirds is motor, and contains the fibres from the

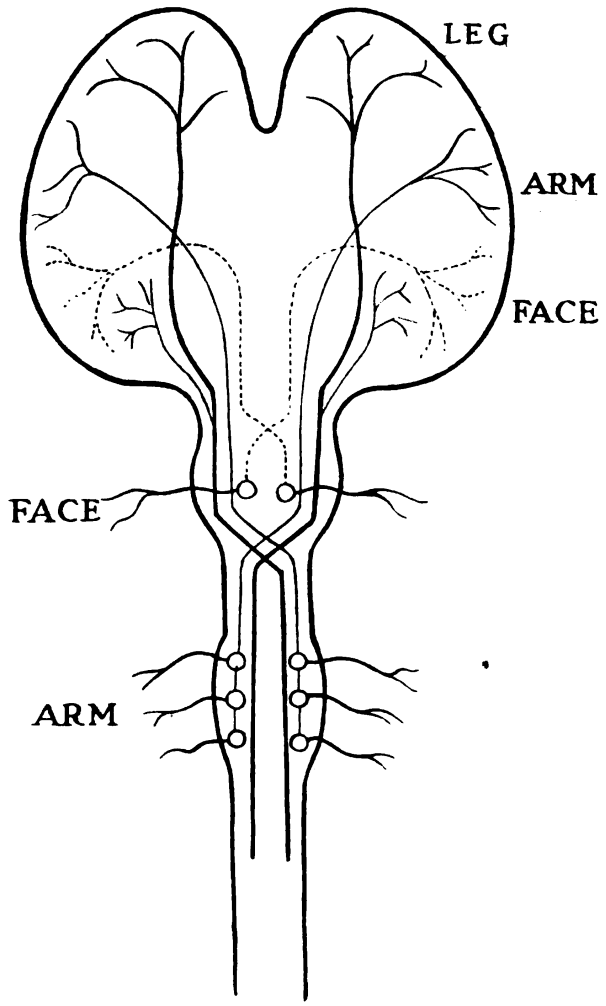

FIG. 2.—Course of fibres from cortex.

motor regions of the cortex, and the posterior third sensory, containing the fibres from the posterior portions of the brain (Fig. 3). It is evident there are two places where hemiplegia of the ordinary kind could be produced: first, on the cortex of the brain by a lesion involving the whole of the motor region; secondly, by a lesion which affects the motor fibres at some point between the cortex and the crus. It is very unlikely that the lesion should be so extensive in the white substance of the brain (the corona radiata) as to involve all the motor fibres equally as they pass inwards from the cortex, but the lesion need be of no great size if it were so seated as to involve the motor fibres where they are concentrated in the internal capsule. A lesion limited to the internal capsule is not probable because it would have to be so small, but the internal capsule might easily be pressed on, or destroyed by a lesion outside it. This is what is meant by capsular lesions—not a lesion limited to the internal capsule, but involving it by pressure or destruction. The term "capsular" is unfortunate, as it is so often misunderstood by students and misapplied.

The next thing that is requisite for a right understanding of hemiplegia is the blood supply to the motor regions of the brain. The blood supply to the brain, you will remember, has its peculiarities. At the base of the brain is what is described as the circle of Willis, and that is formed by the internal carotid and basilar artery with anastomosing branches between them. The circle of Willis, however, has but little bearing upon the question of hemiplegia. It is the internal carotid and its branches which are of prime importance in this connection. The internal carotid, turning up from the floor of the skull after giving off the anterior cerebral artery to supply part of the frontal lobe and the posterior communicating artery to assist in forming the circle of Willis, turns outwards to run in the Sylvian fissure, where it is called the Sylvian artery. Just before this it gives off a group of vessels which perforate the brain and are called perforating arteries.

If you separate the lips of the Sylvian fissure you will see the Sylvian artery lying in it upon the island of Reil, and giving off various branches to the adjacent parts of the brain above and below: a small one to Broca's convolution, a large one running up the ascending frontal convolution, a similar one running up the ascending parietal convolution, *i.e.*, one on each side of the fissure of Rolando, and others which supply the supra-marginal and angular gyri, while smaller branches are given off below to supply the convolutions of the temporo-sphenoidal lobe. Thus the Sylvian artery supplies the whole motor area of the cortex of the brain, as well as some other parts which have to do with the special senses of sight and hearing. Exactly corresponding with the localisation of motor function in the cortex in the brain there is, then, this very

peculiar blood supply, and it is evident that by cutting off the blood supply by these vessels, it would be possible to produce such an effect upon the whole motor area as to cause hemiplegia. We may conclude, therefore, that the most likely cause of cortical hemiplegia would be obstruction to the Sylvian artery. Embolism and thrombosis are the two most likely causes of such obstruction. Consequently, if in a given case there is reason to believe that the cause of the hemiplegia is embolism or thrombosis the most likely seat of the lesion is the Sylvian artery, and the hemiplegia is of cortical origin (Fig. 4).

rhage here would not of itself cause hemiplegia, but as the hæmorrhage would lead to pressure all around, the internal capsule which surrounds the lenticular nucleus would be pressed on, and thus hemiplegia be produced. If the hæmorrhage was small as the clot consolidated and the serum was absorbed, the pressure on the internal capsule might be relieved and the hemiplegia be very transient. If the bleeding extended, reached the internal capsule and more or less tore it, the consequent paralysis would be more or less permanent.

From what has been said of these perforating arteries it is clear that there is no one of them

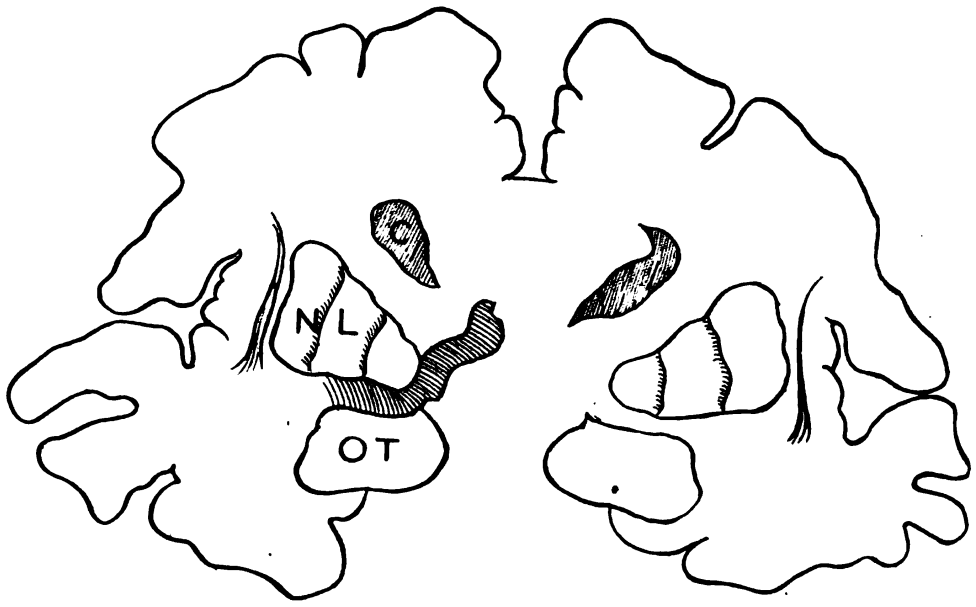

FIG. 3.—The internal capsule is the Y-shaped tract between the lenticular nucleus (N L) and the caudate nucleus (C) in front and the optic thalamus (OT) behind. The shaded portion of the posterior limb (the anterior two thirds) contains the motor tract.

The perforating arteries run straight into the brain, supplying the parts near which they run, viz. the large basal ganglia and internal capsule (Fig. 5). There are two large branches which appear on section in the posterior part of the internal capsule, and run forward some distance—one outside the lenticular nucleus in the external capsule, and another running through the lenticular nucleus to supply it and the anterior part of the internal capsule terminating in the caudate nucleus in front. This is an important vessel, and was named by Charcot the artery of cerebral hæmorrhage, because it is this vessel which commonly gives way in apoplexy. When this vessel gives way the bleeding will first take place in the lenticular nucleus. A hæmorrhage which alone supplies the internal capsule, obstruction of which could cause paralysis as in the case of the Sylvian artery. Morbid anatomy, moreover, shows that embolism or thrombosis of the central vessels is practically unknown, except where the main trunk of the middle cerebral artery is involved.

Two very important conclusions follow from this account of the circulation in the brain; first, that if the cause of the hemiplegia be hæmorrhage, the lesion will be found in all probability in the central substance of the brain; but if embolism or thrombosis be the cause the vessel involved will be the Sylvian artery, and the lesion be not central, but cortical.

Let us now address ourselves to hemiplegia from the clinical point of view. The patient has paralysis of leg, arm, and face, so that the general diagnosis is easy.

The common causes of hemiplegia are hæmorrhage, thrombosis, and embolism. How are we to find out now which of these it is? Rupture of a vessel leads to sudden extravasation of blood. This will increase the intra-cranial pressure enormously. Cerebral compression or pressure, it does not matter whether it be inside or outside the brain, if it be sudden will cause the patient to be unconscious. In the case of embolism and thrombosis, where the vessel is merely plugged and the circulation stopped, there is no increase of pressure, but on the contrary, if anything, a decrease; we can thus distinguish between hæmorrhage and obstruction of vessels by ascertaining whether the patient was or was not unconscious at the time of the attack. If the patient were unconscious for any length of time after the attack the cause was hæmorrhage. If the patient were not unconscious at all, or only for a very short period, it is clear that the cause was not hæmorrhage. Having decided that the cause was not hæmorrhage owing to the absence or slight degree of unconsciousness, we have next to decide whether the cause was embolism or thrombosis. An embolus is generally a fragment of clot, and the source of the clot will generally be found somewhere in the heart. You will therefore examine the heart, and if there be a lesion there you will conclude that the hemiplegia is due to embolism. If no lesion be found to which an embolus can be traced, the cause of the hemiplegia will probably be thrombosis, *i. e.* a clot formed *in situ*. But thrombosis can hardly occur in a healthy vessel, and the further question then arises, What evidence is there that the vessel is diseased? There are severe affections of vessels which may lead to thrombosis, just as they may to hæmorrhage. One very common in elderly persons is atheroma, a senile change. Another is associated with granular kidney, which, however, is not nearly so common a cause of thrombosis as it is of hæmorrhage. Another very common one is syphilis producing what is called "syphilitic endo-arteritis." And there are some septic affections which produce what may be called "septic arteritis." Thus the vascular lesion which has determined the thrombosis or hæmorrhage as the case may be in an elderly person will probably be atheroma, in a middle-aged person granular kidney, and in a younger person it will probably be syphilis.

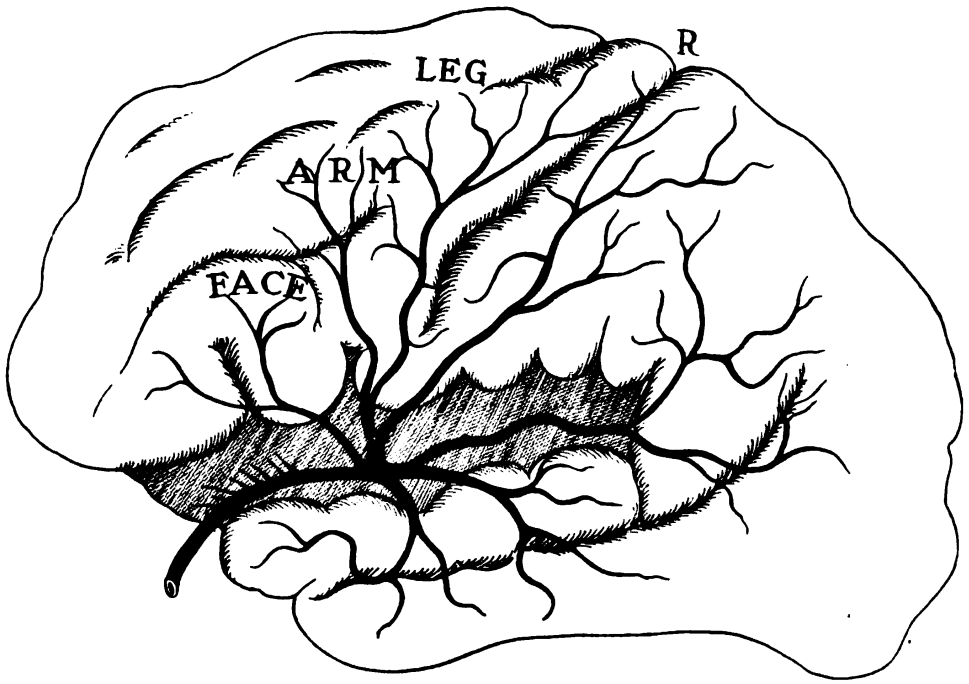

FIG. 4.—Fissure of Sylvius opened out. Sylvian artery and its branches distributed to motor centres on cortex.

Now you see how simple the question becomes when the facts are grasped. A patient has hemiplegia; you ascertain whether at the time of the

attack the patient was unconscious or not; if he was unconscious for some time there must have been cerebral pressure, and that means hæmorrhage, and the seat of lesion will be in the centre of the brain. If the patient was not unconscious then it has not been hæmorrhage but embolism or thrombosis, and the lesion is cortical.

One or two points about prognosis may now be considered, because prognosis depends, as it ought, largely upon pathology. In prognosis there are three questions involved:

(1) Is there any immediate risk to life?

(2) Will the patient recover, and how far?

(3) Will his expectation of life (*i. e.* the probable duration of life) be shortened?

vessel which led to the hæmorrhage, however, remains; consequently there will be a tendency to recurrence, and the prospects of living long be thereby considerably reduced.

In vascular obstruction, *i. e.* embolism or thrombosis, the prognosis as regards immediate danger to life is small, and such cases rarely terminate fatally. On the other hand recovery is rarely, if ever, complete, for obstruction must have been considerable to have produced hemiplegia at all, and if the vascular supply is cut off from the nervous tissues for a very short time only the nutrition of the parts is profoundly disturbed, and the damage done is hardly ever completely repaired, though recovery will probably take place up to a certain point. In

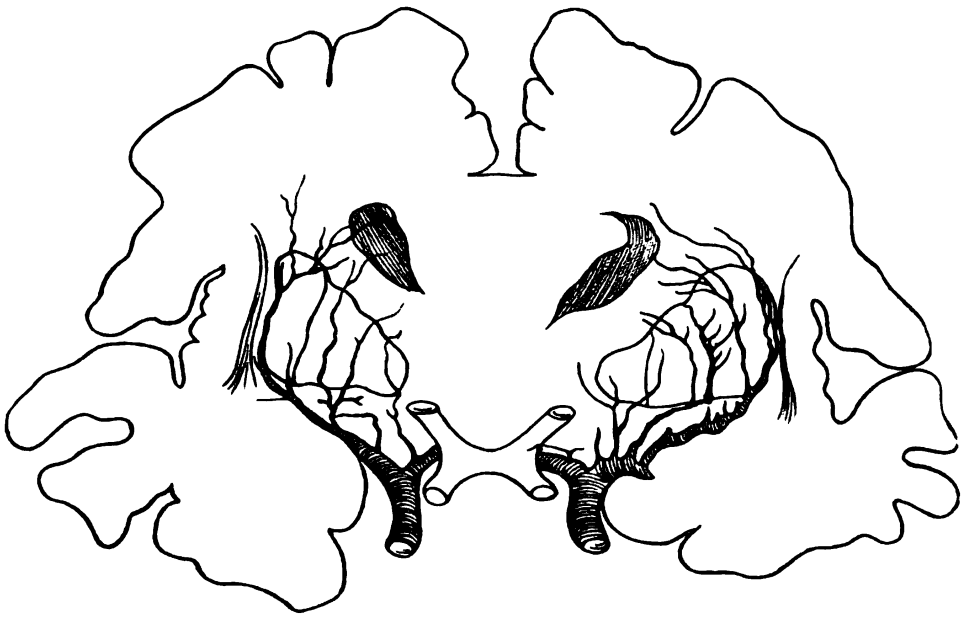

FIG. 5.—The perforating branches of the middle cerebral artery.

In cerebral hæmorrhage the danger to life depends upon the amount of hæmorrhage, and this may be measured by the degree of unconsciousness. So long as the patient is profoundly unconscious, that is to say in an apoplectic condition, the risk of death is considerable. The degree to which recovery will take place will depend upon the damage done by the hæmorrhage. If the hæmorrhage has been small, so that the internal capsule is only pressed on and not torn, so soon as the blood is absorbed and the pressure relieved the symptoms, *i. e.* the paralysis, will rapidly pass away; but if the brain substance and internal capsule have been torn by the hæmorrhage, the damage done is permanent and the paralysis will persist. The disease of the

these cases too, as in hæmorrhage, inasmuch as the disease which led to the paralytic attack persists there will always be the chance of recurrence, and the prospects of living will be seriously diminished.

There remain to be considered a few general questions in respect of treatment. We talk of treating a case of hemiplegia, and so we do, for we can treat the case, *i. e.* the patient, even if we cannot do much for the disease. By the time you see the patient in a case of hemiplegia, the damage has been done. If it be due to hæmorrhage a large part of the brain has been ploughed up by the blood, and you cannot undo that. If you see the patient early when the hæmorrhage is beginning you may do something by

bleeding, but bleeding, if it is to be of any use at all, must be free, and continued till a definite fall in blood-pressure is produced. As soon as that occurs a clot may form in the bleeding vessel and the hæmorrhage be stopped. I have bled in early cerebral hæmorrhage many times, and I am sure I have saved life by that means more than once, but it is no good bleeding unless you reach the case early. When patients come under treatment at a later stage, whatever be the original cause of the attack you can do nothing else than treat them in a general way, by placing them under the best conditions for the damaged nerve-fibres to recover, by maintaining the nutrition of the muscles by massage and electrical stimulation, by treating in appropriate ways the disease of the heart or vessels which led to the attack, and lastly, by so regulating the patient's life as to diminish the chances of recurrence.

The understanding of ordinary hemiplegia depends, then, upon the knowledge of a few elementary facts of cerebral anatomy and physiology. These facts will assist you to comprehend other cases of brain disease, *e.g.* tumours, in which hemiplegia, more or less incomplete, is a symptom.

June 14th, 1909.

Medical Golfing Society.—The annual tournament of the Medical Golfing Society will be held at Burnham Beeches Golf Club on Thursday, June 24th. Play will be eighteen holes match play *v.* Bogey under handicap. There will be three prizes in each division—handicap 12 and under and handicap over 12. The "Henry Morris" Challenge Cup and the Medical Golfing Society's Gold Medal will be competed for. There will also be a Foursomes sweepstake in the afternoon. Any person on the Medical or Dental Registers can join on payment of the annual subscription (four shillings), which includes entrance to the tournament. Entries, accompanied by subscription and giving lowest handicap, should be sent to L. Eliot Creasy, 36, Weymouth Street, London, W., on or before Monday, June 21st. Conveyances will meet trains at Burnham Beeches Station (G.W.R.). Cards may be handed in till 8.30 p.m. Competitors who may be unable to spare the whole day can leave Paddington Station by the 4.40 afternoon train, and arrive at the Burnham Beeches Golf Club in time to play a round and hand in a card by 8.30. It may be useful for players to know that the telephone number of Burnham Beeches Golf Club is 050 Burnham, Bucks.

A CLINICAL LECTURE

ON

HÆMOPTYSIS AND ITS TREATMENT.

Delivered at the Medical Graduates' College and Polyclinic.

By J. EDWARD SQUIRE, C.B., M.D., F.R.C.P.,
Physician Mount Vernon Hospital for Diseases of the Chest; Consulting Physician, Sanatorium for Workers, Bevenden.

BLOOD-SPITTING is almost invariably an indication of disease, and can never be safely disregarded, however small the amount of blood which is expectorated. In every case a careful attempt should be made to discover the source and cause of the bleeding.

Patients frequently attempt to find excuses, as it were, for the hæmorrhage, suggesting some possible explanation in the hope that it may be considered adequate, and that their fear of some more serious reason for the blood-spitting may prove to be groundless.

A man tells you that after a hot day's cricket, during which he over-strained himself by bowling, he coughed up some blood—the probability is that he has commencing tuberculosis of the lung, and that the over-exertion has resulted in a warning which, if not disregarded, may lead to treatment whilst the condition is still curable. A healthy lung does not bleed from strain of this kind. Another person will attribute the hæmorrhage to the effect of lifting a heavy weight; still another explains it as the result of straining with the cough of a temporary cold, or it "comes from the throat," which is congested with much speaking or from smoking. A young woman spits up blood at or about the menstrual period, and looks upon it as merely a result of the general tendency to hæmorrhages at this period. I have come across several such cases of "vicarious menstruation," but there has always been tuberculosis of the lung, early or advanced. All the above examples and various other suggested explanations have come within my own experience, where examination has revealed the true cause in tuberculosis of the lung. Many such warnings, which might have given early

indication of commencing consumption whilst still curable, have been overlooked because some trivial accident, which determined, but did not primarily cause, the bleeding, has been accepted as a sufficient explanation of the hæmorrhage. It is wise not to accept these "excuses," or to be satisfied with any suggestion of some unimportant accidental cause, unless you are able, after careful inquiry and examination, to exclude the more serious but much more common causes of hæmoptysis. So rarely is hæmoptysis due to unimportant circumstances as compared with the frequency of its dependence upon pulmonary tuberculosis that it is not always wise to accept your inability to detect any physical signs of disease as proof that there is none. The blood-spitting is too important a danger-signal of possible—or rather of probable—mischief to be dismissed because signs corroborating the suspicion are not immediately apparent. It is possible that to the well-trained ear there may be already signs in the chest which will indicate the nature and site of the mischief. Remember the importance of early treatment in tuberculosis of the lung, and do not remain inactive in order to allow time for the signs to develop.

Sudden unexpected hæmoptysis is frequently the first indication of tuberculosis of the lungs, and the cases which commence in this way are often the most hopeful, because the fright of the hæmorrhage sends the patient to seek advice without delay.

But though hæmoptysis is most commonly a symptom of pulmonary tuberculosis (consumption), it occurs also in other diseases of the lungs and in diseased conditions unconnected with the lungs.

The following conditions are amongst the possible causes of hæmoptysis:

In connection with the respiratory organs we meet with hæmorrhage in malignant disease of the lungs, in hydatid of the lung, and occasionally in emphysema, bronchiectasis, or pleurisy. It is, of course, one of the consequences of injury to the lung, as from fractured ribs.

In connection with the circulatory system hæmoptysis may occur in mitral disease of the heart (especially stenosis), it may result from morbid conditions of the blood, such as leukæmia, scurvy, purpura, or hæmophilia, and it is possible that slight hæmorrhages may be produced by vaso-motor disturbances. Severe and often fatal hæmoptysis occurs when an aortic aneurysm bursts into the air-tube.

Liver disease—cirrhosis or abscess—may be accompanied by hæmoptysis, as may also Bright's disease of the kidneys.

Blood may get into the mouth (and be spat out) from the throat or pharynx, from the gums, or from the stomach, and in the latter case the hæmorrhage may be severe.

Bear in mind that though blood from the stomach may be dark and clotted if it has been retained for a time within that organ, blood from either stomach or lung may come out at the mouth clear, bright, and liquid, so that it is impossible from the appearance of the blood to tell its source. Small hæmorrhages are often referred to the pharynx or throat, but although this may be a correct explanation it should not be accepted without adequate evidence. Some three years ago a patient of mine, who had had consumption which had become (and still remains) arrested, was alarmed by finding blood in the phlegm he coughed up first thing in the morning as the result of a cold (catarrh). I could not find any signs in the lungs to suggest renewed activity, and at length one morning when I saw him I was fortunate enough to find a small blood-clot still adhering to the dilated vein in the back of his congested pharynx from which the bleeding had occurred, thus conclusively clearing up any doubt there may have been as to the source of the blood.

The amount of blood expectorated from the lungs may vary from a small speck or streak in the phlegm to several pints. The large hæmorrhages are most likely to occur in tuberculosis or malignant disease of the lung or from an aortic aneurysm. In consumption severe hæmorrhage more usually occurs in the advanced stages of the disease, especially when cavities are present in the lung. In this latter case the blood comes from the rupture of a blood-vessel, often the seat of an aneurysmal dilatation, in the wall of the cavity or stretching across the excavation, or from ulceration of a vessel in the course of softening and excavation.

In the earlier stages of tuberculosis (as also in those cases where hæmoptysis occurs in heart or liver disease or in scurvy, etc.) the blood oozes from congested vessels and ruptured capillaries. Although capillary bleeding is often of com-

paratively small amount, we occasionally meet with very severe hæmorrhage in these cases.

When hæmoptysis occurs in the course of a well-established disease it should not be difficult to determine its cause. Thus hæmorrhage from disease of organs other than the lung rarely occurs until the disease is well advanced and its presence already known. So also in advanced consumption the physical evidences of the disease will be well marked. In malignant disease or hydatid of the lung, too, signs of marked physical changes in the lung will probably be evident on examination of the chest, although we may not always interpret them correctly.

I have, comparatively recently, seen in consultation two cases of malignant disease of the lung which were taken for simple cases of pleurisy with effusion until hæmorrhage occurred and suggested a diagnosis of tuberculous pleurisy. In both these, secondary growths occurred in other organs before death.

It is in the early stage of pulmonary tuberculosis that hæmoptysis is of such importance as an indication of disease. An attack of hæmorrhage may be the first sign which causes alarm, or even the first hint of anything being wrong. If the amount is small and if the hæmorrhage is not repeated the warning may be disregarded. I saw recently a lady who was anxious about her health, but on examination I could detect no evidence of active disease in the lungs. I, however, told her that I found signs of past mischief (a scar in the right apex). She then for the first time informed me that eighteen months previously she had an attack of hæmoptysis, but as this did not recur she did not seek medical advice. Fortunately she got over her attack of consumption, as many people do, but as the attack had occurred comparatively recently it was necessary to advise care for another year or two.

I have already drawn attention to the importance of looking upon all unexplained cases of blood-spitting, however small the amount, as probable cases of pulmonary tuberculosis. External circumstances which are sometimes offered as explanations of the bleeding are generally only determining causes. Such are excessively hot weather, sudden strain, over-exertion, or lifting weights.

Hæmoptysis—slight or severe—is said to occur at some time in the course of the disease in from 50 to 80 per cent. of all cases of pulmonary tuberculosis. It is, therefore, in consumption that we shall most frequently meet with hæmoptysis. As already noted, it may be the first apparent sign of ill-health. Occasionally the individual has not even experienced the lassitude and general indefinite malaise which often alone marks the commencement of pulmonary tuberculosis. There may be no warning of anything unusual until a sudden cough brings up blood-stained sputum or pure blood. Sometimes the patient is attacked during sleep, and waking with a saltish taste finds there is blood in the mouth.

The amount of blood brought up at this early stage is often small, but even the initial hæmoptysis may be considerable as it frequently is in the later stages of the disease. The larger hæmorrhages may be preceded for a day or two by some slight staining of the phlegm, and by giving the patient, who has such stained expectoration, complete rest for a few days, a more severe hæmorrhage may be avoided. The following figures, which I have obtained from the Mount Vernon Hospital, where the precaution is taken of keeping all such slight cases in bed, bears upon this point. Out of 2611 patients in the Hospital during 1906, 1907, and the first three months of 1908, there were 183 cases of blood-stained sputum, of which 17 only went on to more severe hæmorrhage; there were during the same time 51 cases of primary hæmorrhage, *i. e.* hæmorrhage without previous staining of the sputum, and there were two deaths from hæmorrhage. In my experience hæmoptysis seems to be more common in males than in females, and to occur less frequently under open-air conditions than when patients were kept in close, warm rooms.

With consumptive patients under continuous observation, as in hospital, it may be sometimes possible to observe some restlessness or other slight change of condition for a few hours or a day or two before an attack, which the experienced nurse recognises as a warning of an impending hæmoptysis. These premonitory signs may be coincident with the actual hæmorrhage in the lungs, the blood being coughed up later. With the occurrence of hæmoptysis the body temperature is often affected: there may be a rise before the attack, there is generally a fall below the normal

immediately after the hæmorrhage, and a rise above the patient's previous temperature may follow quickly after. In some cases, after a few days of normal temperature, or, at least, of similar temperature range to that before the hæmoptysis, there may be a notable rise with subsequent hectic or septic irregularity. This indicates an increased activity of the tuberculous process, or some septic infection producing a septic broncho-pneumonia. It seems as if some of the blood, having gravitated into the more dependent portions of the air-tubes and lung, had there served as a culture medium for tubercle bacilli or septic organisms.

The expectoration of blood may not exactly coincide with the actual hæmorrhage in the lung; the blood may be retained for a time within a cavity or air-tube before it is coughed up. Similarly blood may be seen in the sputum for several days after the hæmorrhage has ceased.

The loss of blood, if considerable, may cause faintness, with pallor, weak pulse, and cold extremities. Even a slight hæmoptysis causes much anxiety and alarm. It is important to reassure the patient as far as possible, and it may be necessary to allay the anxiety—or at the least to deaden the appreciation of it—by sedatives, such as morphine. Fortunately we can truthfully assure the patient that there is little danger; death during, or as a direct result of, an attack of hæmoptysis is comparatively rare—only two deaths in 135 cases of hæmoptysis in the figures given above from the Mount Vernon Hospital. Even two or three pints of blood may be brought up without fatal result.

The capillary hæmorrhage of the early stages of consumption, is rarely fatal and most frequently produces no ill-effects; it is the hæmoptysis of chronic comsumptives, especially where there are large cavities in the lung, which are the more dangerous.

When hæmoptysis does prove fatal, this may be from suffocation due to the large amount of blood coming quickly and filling the air-tubes, or it may be after the attack from exhaustion.

Treatment.

Every case of hæmoptysis should be treated as a serious condition. Absolute rest is essential during the continuance of the bleeding and for some days after all signs of blood have disappeared from the sputum. The patient should be put to bed, if not already there, on the first appearance of blood. It used to be the constant practice to make the patient lie as flat as possible, the pillows and bolster being removed. Instead of this we now prop the patient up, raising the head and shoulders. The application of ice to the chest is also discarded, though the patient may have ice to suck. The loss of blood causes thirst, which may be relieved by sucking ice more safely and more satisfactorily than by giving large quantities of liquid to drink.

The treatment of hæmoptysis must be guided by a knowledge of the cause of the hæmorrhage. I recently saw in consultation a case of severe hæmoptysis in a consumptive girl, which had not yielded to ordinary treatment. I found the right chest to be almost full of fluid, and prescribed saline purgatives and diuretics, by the aid of which the pleural fluid became absorbed and the hæmorrhage ceased. Since, however, the majority of cases depend upon conditions which are common to many consumptives, it is allowable to speak of a "routine treatment" for hæmoptysis which will be found of service in the great majority of cases.

The following remarks are based upon the practice followed out at the Mount Vernon Hospital.

The treatment of hæmoptysis may, for convenience of description, be divided into three, viz.:

(1) Prophylactic.

(2) Acute hæmorrhage.

(3) Subsequent to acute hæmorrhage.

Prophylactic.

If the smallest amount of blood staining is noticed in the sputum it should be looked on as a danger signal, and the patient ought at once to be put to bed. Calomel gr. ij, iij, or iv should be given, depending on the patient, followed in the morning by ʒj or more of mag. sulph.; if necessary this may be repeated in the day. The patient remains in bed for a couple of days, taking the mag. sulph. each morning, and if no more staining appears he is allowed to get up, beginning with two or three hours the first day.

If the staining continues the above treatment is given, the amount of milk may be reduced to one pint daily, and he is of course kept in bed till the sputum is clear for at least three days.

Acute Hæmoptysis.

This is treated by propping up the patient in bed. Amyl nitrate ♏x to xv is inhaled. In a slight hæmorrhage this is usually sufficient. Smaller amounts than ♏x do not usually have much effect.

In larger hæmorrhages, particularly where the nose gets blocked up with blood, it may be necessary to put from ♏xxx to lx on a piece of lint and hold it over the patient's mouth. This has in some cases been repeated, and the only complaint the patient made was that it produced a feeling of sickness.

Turpentine (about ♏xxx to lx) may be used as an inhalation where amyl nitrate is not at hand, or spirits of turpentine (♏x to xxx) may be given internally and repeated. Turpentine is an old remedy for hæmoptysis which still remains one of the most reliable and efficacious. A little care is required in its administration, as suppression of urine may result if the drug is used too long or in excessive doses.

Morphine has been given with good results in slight cases; its action is probably due to the relief of anxiety from the sedative, with consequent quieter action of the heart.

Adrenalin (♏v of a 1 in 1000 solution) has been injected. There seems to be considerable diversity of opinion as to the value of adrenalin—or hemisine—in hæmoptysis. It is said to be useful in cavity cases where it is likely that the hæmorrhage is due to the erosion of a medium-sized vessel. On the other hand it is said to be contra-indicated when the hæmorrhage is from a ruptured vessel, but is useful in congestive hæmorrhage.

It is said to stimulate the sympathetic nervous system, and in this way to cause constriction of all the smaller arteries; the arterioles of the lung are not supplied with constrictor fibres from the sympathetic system, and should therefore be unaffected by adrenalin.

Thus adrenalin is theoretically distinctly contra-indicated in pulmonary hæmorrhage, for its use will raise the general systemic blood-pressure and leave the pulmonary blood-vessels unconstricted.

It should be a general rule that when the hæmorrhage is large and a cavity is known to be present, the patient should be made to lie on the side on which the cavity is.

Subsequent to Acute Hæmorrhage.

The patient is kept in bed, if possible, propped up a little. Purgatives, beginning with calomel from gr. ij to iv are given, followed up by mag. sulph. one, two, or three times times daily; the amount and time must depend on patient's condition.

Milk, one pint, must be given in twenty-four hours, and all other fluid cut off as much as possible, and the patient fed on solids.

In some cases calcium lactate gr. xv has been given *t.d.s.* for three days and then omitted for three days, and so on. Or calcium chloride gr. x to xlv in water or milk, every four to six hours, may be given in a similar manner.

These calcium salts increase the coagulability of the blood and thus tend to check hæmorrhage.

The following prescriptions have also been found useful in continuous hæmoptysis:

℞	Tr. digitali	♏iv
	Tr. hamamelis	♏x
	Tr. ergot. ammon. . . .	♏xx
	Calc. chloridi	gr. x
	Aquæ menth. pip . . .	℥j
	℥j *t.d.s.*	
℞	Liq. trinitrini	♏j
	Spt. ether. nit.	♏x
	Spt. chloroformi	♏v
	Aquam ad	℥j
	℥j *t.d.s.*	
℞	Calc. hypophos.	gr. x
	Acid. phos. dil. .	♏x
	Tr. cinchonæ co. . . .	♏xxx
	Aquam ad	℥j
	℥j *t.d.s.*	

We sometimes come across cases in which hæmoptysis keeps on with only slight intermissions for several weeks, and nothing appears to do any good.

The general principles of treatment may be summed up as follows:

Get the patient to bed, endeavour to calm his anxiety, endeavour to determine the cause of the hæmorrhage, and let your selection of drugs be guided by this.

It is not wise to examine the chest too fully nor too frequently during or immediately after an attack of hæmoptysis.

June 14th, 1909.

TREATMENT OF SCOLIOSIS.

A. STEINDLER considers that while a number of good and practical corsets have been made which give approximately satisfactory results, it is somewhat difficult to meet the two most important requirements, the one of giving a reliable and uniform support to a deformed spine, the position of which has been improved by mechanical or gymnastic treatment, and the other of exerting a correcting influence on certain parts of the body by means of the corset itself. In cases in which there is considerable shifting of the body to one side, for instance in which the lumbar part of the spine is primarily involved in the curvature, not enough hold may be gained for correction and the maintenance of the corrected portion. He has devised an apparatus which he describes: "The sideward shifting of the body will always result in a lifting of the pelvic belt of the corset from the iliac crest of the opposite side, unless its position there is otherwise secured. In order to obtain this advantage, and, on the other hand, to exert some correction on the costal prominence, I attached to the pelvic belt on the healthy side a thigh-piece connected with a hinge and embracing the leg by means of a padded ring right above the knee. On the side of the scoliosis a pad corresponding to the costal prominence articulates by means of a hinged steel piece with the pelvic belt, a similar pad being attached on the corresponding anterior costal prominence of the opposite side. On both pads a considerable amount of elastic pressure is secured by a couple of springs. It is easily to be seen that, if the attachment to the leg is given, bent decidedly outward, and then fastened closely above the knee, an opposite movement of the pad will result in bringing the sideward shifted body over the median line to the other side. Two uprights in the back on both sides of the spinous processes give the body rest and allow the shoulders to be pulled back by shoulder-straps." The patients had been given mechanical treatment, gymnastic and otherwise, which was continued after the application of the apparatus. Steindler had, to a great extent, given up mere extension as a method of correcting curvature.—*Medical Record*, vol. lxxv, No. 22.

ANURIA.

KÜMMELL records his experience with anuria at Hamburg, and emphasises the necessity for regarding anuria as a very serious condition, not to be neglected any more than acute ileus or incarceration of a hernia. The patients sometimes experience apparently no ill-results; in one of his cases the patient felt perfectly well, notwithstanding four days of total anuria from obstruction by a kidney stone, and was with difficulty persuaded to allow an operation. In one case the anuria persisted for twenty, and in another for thirty days, and normal urination was then spontaneously restored. These are the rare exceptions; the anuria, as a rule, entails a comatose uræmic state after a phase of subjective freedom from disturbances. Anuria from renal concretions offers a grateful field for treatment when recognised early. If the X rays show the stone to be too large to anticipate its expulsion by the natural routes, operative intervention should be advised at once without further waste of time. If not larger than a cherry-stone, or if its shape permits the hope of spontaneous expulsion, the ureter should be catheterised in the hope of dislodging the stone or stimulating the ureter to more energetic peristalsis, with or without injection of oil or glycerine through the catheter. Casper succeeded in stimulating the ureter by injecting water into the kidney pelvis on the other side, the reflex peristalsis thus induced becoming so vigorous that the uncatheterised ureter expelled the obstructing stone. Kümmell advises the use of the ureter catheter whenever indicated, but if no effect is promptly realised he would not waste further time on it, but proceed at once to the operation. In case there is obstruction in both kidneys his experience confirms the advisability of operating first on the kidney last obstructed. In case the wrong kidney is exposed by a mistake in diagnosis, he advises opening up at once the other kidney and removal of the concretions. If the stone is in the ureter and the obstruction is comparatively recent it may be unnecessary to open the kidney, but if the obstruction is of long standing the kidney above is necessarily altered: also if the patient is comatose when first seen the kidney should be incised. In his nine cases of concrement anuria in three patients there was only one kidney in each, and these individuals all died, although one might have been saved by prompt removal of the stone. In all his cases the trouble was so advanced that operative intervention had scarcely any chance. The prospects are less favourable with anuria resulting from disturbances in the circulation; internal measures are indicated here, diuretics, saline infusion, venesection, and in extreme cases, decapsulation of the kidney.—*Journ. A. M. A.*, vol. lii, No. 22.

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A CLINICAL LECTURE

ON

SHORT CIRCUITS OF THE LYMPHATICS IN CANCER OF THE TONGUE, BREAST, AND ORGANS OF GENERATION.

Delivered at St. Bartholomew's Hospital.

By C. B. LOCKWOOD, F.R.C.S.,
Surgeon to the Hospital.

GENTLEMEN,—I propose to lecture to-day upon a subject which I have already referred to more than once. But I am not afraid of repetition. A great French teacher was once asked how he obtained his successful results, and he replied, "By everlasting repetition." The subject is short circuits in malignant disease of the lymphatic system. The word "short circuit" is one which I borrowed from the electricians. Everyone nowadays is sufficiently conversant with the science of electricity to know what is meant by a short circuit. You are aware that when an electric current is passing from one point to another through a copper wire, if a piece of copper wire is laid across the loop the current will follow the shortest route and cease to pass by the longest. After malignant disease has begun in any organ, it speedily passes into the lymphatics, and pursues the course of the lymphatics onwards towards the thoracic duct and into the general circulation. But if it begins in some part of an organ, and if from that particular part of the organ a lymphatic trunk passes onwards towards the heart and empties itself into the main lymphatic channels nearer to the heart, then the carcinoma will not take its usual long route, but will pass along the short circuit to glands some distance perhaps from the original focus, yet much nearer to the heart than you would suspect them to be. I propose first to draw your attention to the short circuit in cases of carcinoma of the tongue,

next to short circuits in cases of carcinoma of the breast, and lastly short circuits in cases of carcinoma of the organs of generation. There is no doubt that the treatment of carcinoma by drugs has made but little progress. At the best they palliate. I am sure if any of you knew that he had carcinoma he would not trust to medication for the cure of his disease. There is no doubt that the only remaining method, the surgical, has given of late better results. I think there are two reasons for this. One is that the cancers are now diagnosed sooner. In the next place, owing to the increase of our knowledge of the morbid anatomy and histology of cancer, and of the distribution of the lymphatics, especially of those short circuits to which I shall d aw your attention, much more thorough and efficacious operations are performed. I refer to the earlier diagnosis of the original disease. If I were asked what the rules of diagnosis usually implanted in the student's mind were, I should say that they are mere text-book diagnoses. The disease as described in most of the text-books on surgery is the disease in quite an advanced stage, when it is almost beyond the reach of efficacious surgery. But you must learn to diagnose these carcinomata before they have got out of hand. Now, the disease begins in some part of the tongue as a minute lump which is very hard. That lump may or may not be painful. But after a while it will degenerate and ulcerate, and then it will become septic. It is absurd to wait until other clinical signs appear. It must be sufficient for you to know that your patient has a small lump or tumour of the tongue, which is ulcerating. And what a trivial matter it is at this stage to remove that ulcer for microscopical examination. Or what a trivial matter it is to apply a little cocaine and remove a portion of the lump and have it microscopically examined, because I should say that microscopical examination would give you unerring information as to the nature of the disease. At that early stage the removal of the growth with a reasonable margin of, say, half an inch round the little lump, ought to give the patient a proper security. But now we come to another point. One of the characteristics of carcinoma is that it spreads from its very earliest beginnings into the lymphatic system, and spreads perhaps very much earlier than people suppose. Presently I will relate to you an instance of the spread of carcinoma from a carcinoma of the mammary gland, which, I think, will convey to your minds the impression that it must spread at the very earliest stages of the growth. I believe myself that, given a patient with carcinoma of the edge of the tongue, say of the size of a threepenny-piece, that by that time it is certain the carcinoma has spread along the lymphatics into the nearest lymphatic glands. Not many months ago I operated upon a patient who illustrated many of the points with most admirable clearness. One of the peculiarities was that the patient was a woman. Never indulge in that form of reasoning which is supposed to be based upon probabilities: "An ulcerated lump of the tongue, the patient is a woman, therefore it is not likely to be carcinoma." Remove it, and see what it is. This patient not only was a woman, but she was comparatively young—her age was thirty-eight. Do not assume that because your patient is young that the lump in any part of the body—tongue, breast, or anywhere else—cannot, therefore, be a carcinoma. Remove it and see what it is made of. There was another point in this patient's history which was interesting. The carcinoma of the tongue was undoubtedly preceded by a period of chronic inflammation of the tongue. In the tongue, in the breasts, in the pudenda, and elsewhere the presence of a chronic inflammation is often the precursor of the carcinoma. I tell you that because you must not minimise the significance of chronic inflammations of the tongue, of the mammary gland, or of any region of the body, but do all in your power to get them well. This patient had a small epithelioma situated on the posterior third of the tongue. I particularly draw your attention to that locality, because, to some extent, it is a clue to the direction in which the carcinoma is likely to spread. You may divide the tongue, for our purposes, into thirds. The anterior third of the tongue includes the tip. The lymphatics from the point or tip of the tongue, pass from the frænum through the floor of the mouth into the glands underneath the chin. Remember that carcinomata situated near the middle line of the body may infect the lymphatics of both sides. A clerk had carcinoma at the tip of his tongue; he had an infection of the submental glands; but he also had infection of the glands of both sides of the neck, and a sweeping operation was done for their removal. The lymphatics of the anterior third of the tongue

pass forward into the submental gland and into the glands in the front part of the sub-maxillary triangle. The lymphatics in the middle third of the tongue pass into the glands on the side of the tongue underneath the submaxillary gland in the substance of the submaxillary gland, and in the submaxillary triangle. The posterior ones pass backwards into the glands in the region of the carotid vessels. A little gland which I have drawn your attention to underneath the submaxillary gland on the side of the tongue is very often overlooked. It is overlooked because it is not properly felt for. I do not mind repetition, and therefore I repeat the manner in which you ought to feel for this gland. Sit the patient up in a chair, put one finger inside the mouth, and another finger outside the mouth, and squeeze them together, and then you will feel this little gland if it is enlarged; it will be hard, and will slip between your fingers. It is overlooked by those who merely put their fingers outside the mouth and try to push upwards. All they do then is to push enlarged glands upwards into the mouth, and they cannot, therefore, be felt. The lymphatics of the posterior third of the tongue nearly all pass backwards and empty themselves into the lymphatics which lie beneath the angle of the jaw and along the carotid sheath. One is called the tonsillar gland. It is large and often infected in inflammations of the tonsil. But these lymphatics are situated higher and under the angle of the jaw. This patient admirably illustrated the next point which I want to make. Her carcinoma was small, and although her neck was thin, and although she was examined over and over again, no lymphatic glands could be felt. Now comes the question, How far are you going to trust your sense of touch for the diagnosis of carcinomatous lymphatic glands? Remember, if you make a mistake upon this point and remove a carcinoma on the side of the tongue, which is a small matter, you have left that patient with carcinoma; she still has carcinoma, and do not try to soothe your minds by saying, when the glands continue to grow, that she has some recurrent disease of the lymphatic glands in the neck. I do not know exactly what the word "recurrence" means, but I think it is simply a cloak for carelessness and ignorance. We could not feel any glands whatever in this woman's neck. If she had enlarged glands they ought to be situated in the posterior part of the submaxillary triangle, and also along her carotid vessels under the angle of the jaw, because you will remember I made the point that the carcinoma was situated far back in the tongue. However, being profoundly sceptical about feeling, I made a complete exposure of the submaxillary triangle and of the carotid sheath, and upon that we found three or four enlarged lymphatic glands. These lymphatic glands were easily removed. We then and there submitted them to microscopical examination, and found them to contain carcinoma.

I now come to the next point. I want to tell you of another precaution which was taken in this patient's case. I am now going to refer to a short circuit which takes place when carcinoma spreads from the tongue into the neighbouring lymphatic glands. When the carcinoma is situated in the middle of the side of the tongue, there is a lymphatic trunk which passes down the side of the tongue, underneath the floor of the mouth, along the hyoglossus, and passes over the hyoid bone and onwards over the ala of the thyroid cartilage. On this trunk as it passes down over the ala of the thyroid cartilage there is sometimes a lymphatic nodule, and hence in cases of malignant disease of the lymphatic glands I have felt enlarged lymphatic glands on the ala of the thyroid cartilage, and before I knew of the existence of this short circuit it puzzled me very much to know how in the world a patient could have carcinoma of lymphatic glands situated on the ala of the thyroid cartilage. We have now got our short circuit trunk as far as the ala of the thyroid cartilage. But it passes down further, and makes a loop far down in the neck below the level of the cricoid cartilage. After descending below the level of the cricoid it loops upwards and turns outwards to the carotid sheath, and empties itself into a lymphatic gland which is situated just above the omo-hyoid muscle. By some that gland is called the omo-hyoid gland. Sometimes I have referred to it as the cricoid lymphatic gland because it is on a level with the cricoid cartilage. This is the precaution which was taken in this patient's case. I did not consider I had completed her operation until my incision had been carried down the side of the neck, so that I could expose the omo-hyoid muscle to see whether her cricoid gland was enlarged. On this occasion I think there was no enlargement of the cricoid gland. But over and over again when looking for this cricoid gland deliberately,

one finds that it is enlarged. See how the piece of anatomy which I have placed before you bears on the plan of your operation. Clearly in operating for the removal of cancerous lymphatic glands it is necessary for your incision to begin beneath the chin. I usually carry mine across to the opposite side, so as to be certain to remove all the submental glands, because the lymphatic system has numerous inter-communications across the middle line. Next, your incision must go back to the carotid sheath because you require to see the carotid glands. Next, your incision must go down to the level of the cricoid cartilage, so as to make quite sure you are not overlooking the cricoid gland. I venture to say that if you have not thought out and are not perfectly familiar with this short circuit which I have described, that the time will certainly come when you will remove a carcinoma from the side of the tongue, you may even remove carcinomatous glands to some extent, but you will inevitably leave a carcinomatous carotid gland low down in the neck.

I now leave the tongue and proceed to draw your attention to a short circuit which is met with in carcinoma of the lymphatic glands in connection with carcinoma of the breast. In its earliest stages carcinoma of the breast is a small, movable, painless lump. It is discovered by an accident. After it has been discovered it becomes, perhaps, a source of anxiety to the patient, and then she will say it is painful. The descriptions of carcinoma of the breast in your text-books are mere text-book descriptions; they refer to carcinoma of the breast when it has become a difficult disease to deal with and when it cannot be dealt with with reasonable certainty. You are to diagnose carcinoma of the breast long before it has got to the stages mentioned in your text-books on surgery. How shall you diagnose a commencing carcinoma of the breast? In the simplest possible way. It is a trivial operation to remove these small nodules under an anæsthetic. A small nodule should be removed with a margin and submitted to microscopical examination, and then you will have positive evidence of the nature of the disease which you have to deal with. Carcinoma of the breast is sometimes preceded by chronic mastitis. I am very suspicious of chronic inflammations of the breast, and on many an occasion I have given an anæsthetic and removed a piece of chronically inflamed breast. And I remember on one o we removed a piece of inflamed mammar and found no carcinoma in it. I was sc however, and removed another piece, and carcinoma in the centre of it. So be caref you assume that chronic mastitis is chronic r and that there is no carcinoma in it. Thi carcinoma of the breast consists of two elemer are of importance. First of all there is the e of the cancer-cells; I do not know what th —they may be epithelial cells. But they spaces and these spaces are lymphatic And these lymphatic spaces communicate w lymphatics, so you can easily understand th the early stages of carcinoma of the br spreads into the lymphatics, and passes alon into the main lymphatic stream. How sc these cancer-cells pass from the little growth into the lymphatics and onwards in lymphatic glands? I can recall a case whi a bearing on this question. A patient ha for a time a mucous discharge from the I think if she had not had this discharge fr nipple she would have been unaware ther anything wrong in her breast. On feeling b the areola a small swelling could be fel infinite difficulty. And now I shall draw attention to the manner in which you examine a patient who is supposed to have lump in the breast. First of all, never of examining the patient in the standing sitting-up position. Place the patient prone, supported on a firm couch. Get the patier some comfortable attitude, and then beg examining the normal breast. Sometime make discoveries there. Examine it wit tip of your finger, pressing steadily the mar gland against the chest-wall. Do not pi up in your fingers—that always makes you there is a lump in the breast. If after steadily over the breast with the tip of the and with the patient lying immobile, you feel any obvious lump, you may be r ably certain there is none. If there i comfort or pain, see the patient again afi interval of time. This patient had a minute under the areola, and we proceeded as I advised you to proceed. When we mad little incision and extracted this lump, whic an ampulla with something inside it, the ar

was cut and was found to have inside it a small carcinoma. I then proceeded to remove the whole of the mammary gland together with the pectoral muscles, and all the lymphatic glands up to the subclavius muscle. Why remove the whole mammary gland if a person has only one little carcinoma? This gland was examined by Mr. Shaw, and he found other patches of carcinoma within it. The next question is, Why remove all the axillary lymphatics glands? Was there any carcinoma in them? On microscopical examination the axillary lymphatic glands had carcinoma in them too. I think that is the earliest carcinoma of the breast I have removed, and yet in that early stage carcinoma was growing in other parts of the mammary gland, and there was already carcinoma in the axillary lymphatic glands. How are you to diagnose carcinoma in the lymphatics? I need hardly say that to put off your diagnosis until you can feel enlargement of the lymphatic glands is mere text-book surgery. You cannot feel these carcinomatous lymphatic glands in the early stages. It is a curious point that sometimes when we remove these lymphatic glands, the larger ones which might possibly have been felt in the examination are found to contain no carcinoma when examined microscopically. But minute ones, which are perhaps the size of No. 1 shot, may contain considerable quantities. Do not trust to your sense of touch for the diagnosis of the presence of cancerous glands. Shall you trust your eyes? You may look at these enlarged glands with your eyes as long as you like, but you will not be able to see carcinoma in them. The microscope is the only thing which will tell you whether they have carcinoma in them or not. How shall you ensure these patients' safety? You will do so by performing the operation which you constantly see performed at this hospital, and that is systematic removal of all the lymphatic area which is fed from the breast.

I am now coming to another point, and it is this, What is the whole lymphatic area supplied from the breast? The bulk of the lymphatics of the breast pass up underneath the pectoralis major into the pectoral glands, and from those glands they pass upwards into the glands along the axillary vein, up towards the clavicle and into the infra-clavicular glands, onwards into the subclavian and so into the right or left lymphatic duct. But now I shall draw your attention to the short circuit which oftens exists in the case of the mammary lymphatics. There is described by anatomists, and certainly ought to be recognised by surgeons, an accessory lymphatic route by which the lymphatics of the breast can short circuit themselves into the main lymph-channels. The short circuit consists of a lymphatic trunk, which passes vertically upwards from the mammary gland and then through the fibres of the pectoralis major, or between the pectoralis major and the deltoid, and empties into the lymphatics beneath the costa-coracoid membrane. And I have no doubt that is the explanation of the fact that sometimes, in the widespread operations which I perform, we discover no enlarged lymphatics in the pectoral region, and perhaps none in the axillary fat, but we discover them high up beneath the axillary vein close to the subclavian muscle. If it is correct, that there is a short circuit which will short circuit cancer from the breast into the higher axillary glands, then it is to be noted that these glands lie underneath the pectoralis major and under the costa-coracoid membrane, where they could not be felt. So the only resort is to do an operation which consists in removing the pectoral muscles and costa-coracoid membrane, to enable you to get at the high glands which cannot be seen or felt. I want to go a step further with regard to short circuiting, because this does not complete the short circuit lymphatics in the case of the breast. In some instances—I do not know how many—the short circuit does not end in the infra-clavicular glands, but the lymphatics pass upwards with the jugulo-cephalic vein over the clavicle, and enter the supra-clavicular glands. Probably this is the explanation of a case which I described elsewhere, in which a patient had advanced carcinoma of the breast removed by the complete operation, and nine months later came back with a greatly enlarged carcinomatous gland behind the head of the clavicle and beneath the sterno-mastoid. I thought this was rather a forbidding gland to extract, but determined it should be done, because you will only cure carcinoma of the lymphatics by hunting them out. So I proceeded to turn back the sterno-mastoid and exposed this gland, and removed it with a considerable amount of ease. That patient had immunity from carcinoma for three years more, after which period she died of

carcinoma in her internal organs. I cannot help thinking that her carcinoma, which you will observe had missed the glands in the subclavian triangle and had entered the gland behind the sterno-mastoid, was an instance of short-circuiting of carcinoma by the lymphatic route which follows the jugulo-cephalic vein. I have not time to say more about short circuiting of the lymphatics in carcinoma of the breast, but in the few minutes which remain to me I want to draw your attention to the short circuiting of the lymphatics in carcinoma of the external organs of generation, male or female.

I regret to say that carcinoma of this region is often brought to our notice at rather an advanced stage. You must not say that is the fault of the medical man, but for various reasons, which I need not enter upon, the patients conceal the fact that they have a small lump or ulcer. It is perhaps painless and causes very little trouble, and they do not seek advice until the disease has reached an advanced stage. Carcinoma upon the organs of generation is almost sure to follow the superficial lymphatics and pass upwards towards the pubes. And here a curious thing happens. The lymphatics in front of the pubes, like those in other parts of the median line of the body, interlace and cross. So unless you were aware of this you might say, Here is a patient with carcinoma on the left side, here are lymphatic glands enlarged in the left groin, and possibly omit to examine the lymphatic glands on the right side, and omit to observe that they are very greatly enlarged, the carcinoma having followed the track of the lymphatics across the middle line of the body by interlacing or by direct crossing. Supposing the carcinoma has got to the pubes, the lymphatics follow the superficial external pudic artery, and the superficial inguinal glands become carcinomatous. From the superficial inguinal glands the carcinoma spreads to the intermediate glands which lie in the meshes of the cribriform fascia, and after that into the glands of the crural canal. That is as regards the superficial lymphatics. But when the carcinoma has attacked the deeper structures it passes into the deep lymphatics, and those follow the deep vessels under the deep fascia, and they run with the deep external pudic under the pectineal portion of the fascia lata. This takes them by the direct route towards the femoral sheath. They pierce this sheath and enter Cloquet's gland, which is in the femoral canal. Some of these lymphatics c always empty themselves into the nearest phatic glands—those at the inner side o femoral sheath—but may pass outwards and themselves into the lymphatic glands not v from the origin of the sartorius muscle. (may pass towards the apex of Scarpa's tri where there is a large gland. I have told y this with a definite intent, namely, that you are aware of these facts you might remove these superficial and deep inguinal through small incisions. Your incision mu planned so as to go down to the apex of Sc triangle and outwards as far as the origin sartorius, or you will leave cancerous lym glands in the patient's body. How great temptation to say, Here is the carcinoma, are the enlarged glands in Scarpa's triangle the cancer is not likely to be anywhere else. if you are aware that the lymphatics empty selves near the origin of the sartorius you wil assume that the inside lump comprises all will look for others at the apex and outer si Scarpa's triangle. The last two are almo easily overlooked as the cricoid gland.

Now I am coming to the point. I have you a brief account of the way in which carci spreads into the superficial and deep ing glands. But there is a short circuit. Inside abdomen behind the Poupart's ligament ther chain of glands which corresponds very close the chain of glands on the outer side of Pou ligament, and these glands are called the crural glands. A very large one is situated behind the outer end of the inguinal canal, an one just outside the so-called internal abdo ring. These are the internal and external crural glands. Deep inguinal lymphatics entering the femoral sheath pass into Cloq gland and onwards into the internal retro-c This is the direct route. But some of them pass up the spermatic cord or the round ligam the uterus into the inguinal canal, and pass on in the inguinal canal. They pass through so-called internal abdominal ring and empty t selves into the external retro-crural gland. a temptation to anybody who has examin patient with carcinoma of the pudenda and cinoma of the superficial and deep inguinal gl to assume that that is all the disease he ha

deal with and therefore to cease the operation. I myself, if I have to deal with any advanced carcinoma of these organs, do not hesitate to proceed further and open the iliac fossa and ascertain the condition of these retro-crural glands. It is a very easy and safe step in the operation. I have said elsewhere that I believe the best incision to make is a semi-lunar one. That semi-lunar flap, with its base above, can easily be extended on to the abdomen so as to expose the aponeurosis of the external oblique above Poupart's ligament. And then an incision can be made through the aponeurosis of the external oblique in the direction of its fibres, and then the fibres of the internal oblique and transversalis can be split, and the fascia of the transversalis exposed. I am describing the operation for ligature of the external iliac artery. On the occasions when I have undertaken this operation I have not been surprised to find enlarged and carcinomatous glands inside the abdomen. But I am sure of this, that had I not been aware of this short circuit I would have omitted to look and see. Pay great attention to these short circuits, because unless I have convinced you that they exist and that they are important you will not have the courage when operating upon cases which perhaps do not appear to be widespread cases of carcinoma to open the abdomen and look for the retro-crural glands. But obviously it is a step which must be taken.

One word I have to say to you in conclusion. This procedure of splitting the muscles does not by any means lead to the formation of a ventral hernia, and I believe it is perfectly safe from every surgical point of view.

June 21st, 1909.

WE have received for notice from Macmillan & Co. an interesting little book, entitled 'Home Nursing,' by Isabel Macdonald. This small volume will prove of use in those numerous cases of sickness where the pecuniary resources of the patient's relations and friends cannot stand the expense of employing highly trained nurses. The teaching is simple, the language is plain, and the style is homely; in fact, the little book is admirably adapted for the use to which it is intended—viz. to secure help and aid for the sick in time of need and emergency.

ON THE TREATMENT OF CARDIAC PAIN.

A lecture delivered at the Medical Graduates' College and Polyclinic.

By ALEXANDER MORISON, M.D.Edin., F.R.C.P.Lond. & Edin.,
Senior Physician to the Great Northern Central Hospital.

BEFORE discussing the treatment of cardiac pain, I think it will be of advantage to mention very shortly some considerations affecting the nature and causes of that symptom which, as we know, constitutes at times one of the most tragic situations with which we as physicians have to deal.

To use a phrase often employed at present, in consequence of its having been used by our philosophic Secretary for War, this subject requires, above all, "clear thinking," in order that we may take effective action.

The factors necessary to the production of pain are—(1) a stimulus or impressor, (2) a receiver or surface impressed, and (3) a perceiver or organ for the realisation of impressions and their reference to the site of stimulation.

This will be found to be a sufficiently convenient analysis of the sensation we term "pain," as it will also be seen that the methods used for its assuagement or abolition will group themselves on these lines.

The factors which play a part in the production of cardiac pain are necessarily those which underlie cardiac action, namely, muscle, nerve, and blood, influenced by the circumstances in which these factors exist and operate when pain arises. Here, again, I hope I shall be able to show that our analysis has practical bearings.

It is not necessary for me as a preliminary to set forth with any fulness the anatomy, physiology and pathology which we find associated with cardiac pain; but I hope I may be pardoned if I recall the leading facts of practical importance which enable us to appreciate the bearings of certain signs, and the *rationale* of our methods of treatment in any given case.

The *cardiac muscle* in such cases may be degenerated and enfeebled, or hypertrophied in texture

and excited in action. It may even be apparently normal in structure, but this is not common.

It is manifest that the mechanism of cardiac pain must vary with such variety in the underlying muscular state, and variety in the mechanism of production implies a difference in the method of relief.

The cardiac *nervous system* in cases manifesting this symptom may also be affected in more ways than one. This system has not always, or, I may say, often, been investigated with the care which in my opinion it deserves, and during the prevalence of the present myogenic wave of thought in cardiology is less likely to receive that attention. But there are some points which must be borne in mind if we would appreciate aright both the signs manifested in different cases and the means we should employ for their relief.

The heart is supplied with nerves by two streams on each side, namely, those by way of the vagi and those issuing chiefly from the second and third dorsal spinal nerves. These mingle in the cardiac plexuses, and are so dispersed that the right and left streams innervate not only the cardiac structures on their own side, but also those on the opposite side. This arrangement has the advantage that, if the nerves on one side are disabled, as in surgical operations on the neck, the heart still remains innervated by the corresponding set on the opposite side. It also explains how a stimulus originating on one side of the heart may, in some cases, find referred radiation on the corresponding side of the body, in others on the opposite side, and in yet others on both sides.

In the majority of cases we know that the radiation of pain is towards the left, but in a smaller number it is limited to the right side. The latter was so, for example, in a case of dextral valvular disease under my care in 1875. A recent writer makes the positive statement that "The symptoms of angina pectoris are invariably associated with lesions on the ventricular side of the mitral orifice" (Mackenzie, 'Diseases of the Heart,' London, 1908, p. 43). The opportunity of observing lesions in the right heart are admittedly much rarer than in the left; but the instance I have cited suffices to prove that the assertion I have quoted cannot be regarded as absolutely correct.

It is well known that, normally, the viscera may be handled without evincing sensitiveness, and that tumours and cysts may at times grow in them without causing any pain. On the other hand, we are familiar with the excruciating pain which attends the passage of calculi along channels such as the hepatic duct and the ureters. What is true of these appears to be no less true, in some cases, of coronary arteries, which may be regarded in a sense as ducts.

We are likewise familiar with the discomfort of a distended hollow viscus such as the bladder or stomach, and with colic in the intestines. The colics all occur in tubes and cavities possessing a muscular coat and are provoked by the nature of their contents, stimulating the nervous endowment of their interior. The character of the contents, as regards density or irritating quality, appears to bear some relation to the degree of pain resulting from the peristaltic or propulsive contraction of the muscular organ engaged.

The interior of some organs under certain circumstances thus appears to be as sensitive as their exterior is insensitive. This also seems to be the case with the heart. I have on a previous occasion published details of a case ('Lancet,' November, 1902) in which repeated severe attacks of angina pectoris proved fatal, and in which I found a small intra-vascular aneurysm in the right coronary artery. In the neighbourhood of this aneurysm I also found an intra-vascular cluster of ganglion cells, internal to the muscular coat, a fact, so far as I know, not mentioned by anatomists, but one which I regard as of very great interest. A nerve ganglion in the intima or inner coat of an artery cannot in all probability have a wholly motor or merely nutritional function.

Quite recently, moreover, I witnessed a post-mortem examination on a man, æt. 59 years, who was sent into the Great Northern Central Hospital as a case, in all probability, of perforated gastric ulcer and placed in a surgical ward for operation; Dr. O. E. Higgins, who sent the case in, however, made the alternative diagnosis of coronary thrombus, having previously observed like symptoms in one associated with this condition. The intensity of the patient's pain and his collapsed condition led to the supposition that the case might be surgical. The pain was sudden in origin, to the left of the lower end of the sternum, radiated down the left arm, and persisted without abatement from 8 p.m. on January 22nd till 7 p.m. on January 23rd when

the patient died. The necropsy was made by Mr. Ernest Shaw, the pathologist to the hospital, and revealed a thrombosis of the right coronary artery, the thrombus being in parts decolourised and adherent to the vessel, and extending for about two inches along it. The heart was enlarged, weighing eighteen ounces, and the cardiac muscle was fattily degenerated. Microscopic examination of the partially calcareous vessel, after decalcification, showed its lumen to be considerably narrowed by thickening of the submuscular coat, while both in the muscular and extra-muscular layers there was considerable leucocytic infiltration. The decolourisation and adhesion of the thrombus indicated its impaction in the vessel for a period corresponding with the duration of the fatal cardiac pain. The patient was a large, stout man with much adipose tissue, and had suffered from time to time, apparently from cardiac pain, before his final thrombotic attack. Both coronary vessels were patent though atheromatous, and in parts calcareous and there was slight atheroma of the aorta itself.

It may be a matter of opinion whether the pain in this case was due to impaction of the thrombus in the vessel, or to interruption of the blood-flow —that is, as to whether the pain was vascular or circulatory in origin. But I am disposed to regard the suddenness, severity, and duration of the pain as produced rather on the lines of the impaction of a calculus than on that of the deprivation of blood-flow to the cardiac muscle, for the left coronary artery was quite patent, and we know that coronary anastomosis is much more free than was at one time supposed to be the case.

The *hæmic factor* in cardiac pain plays its part by alteration in the character of the blood, by abnormality in its distribution to the walls of the heart, or by defect in its circulation through its chambers.

But, these factors in cardiac action do not play their part singly in the production of pain. They may all be associated in a given case in producing that phenomenon, and the methods undertaken for the relief of this symptom will in such cases, like the underlying factors, be likewise complex, that is, they will be directed towards a modification of the action of such combinations of the muscular, neural and hæmic factors, as are indicated by a careful study of the clinical signs in a given case to be operative in producing the cardiac pain manifested in that instance.

Cardiac pain, the dolor or angina pectoris of Heberden, may be met with in all degrees of severity, continuousness or recurrence. The term *angina sine dolore*, introduced by Gairdner, can, I think, only be correctly employed if we translate angina as anxiety, fear, or apprehension. With this sense of impending death I shall in no way deal to-day. It is not necessarily limited to cardiac disorder. We are concerned at present with physical pain, mild, moderate, or excruciating in degree, and dependent upon an anatomical lesion in, or abnormal condition of, some component or components of the heart, and which may be comprehensively described as cardiac pain.

The sensory disturbance of the heart may in some cases be so little referred by the patient to the organ itself as to be manifested only by peripheral discomfort in the arm, behind the shoulder, or on the anterior surface of the thorax, usually in the area of distribution of the second and third dorsal nerves. Occasionally the peripheral discomfort may alone be observed, but this is generally followed by definite retro-sternal or præcordial pain. As a rule, however, cardiac pain is most felt in the præcordia, and frequently, although by no means always, radiates thence, and usually, as I have stated, towards the left.

This sinistral radiation even occurs when the causal lesion is in the right coronary artery, and can only be explained by the decussation of the cardiac innervation of which I have spoken, and by the higher blood-pressure in the left side of the heart and systemic arteries.

The right side of the heart is, moreover, more easily distensible than the left, and there appears to be a certain safety-valve action or physiological insufficiency of the right auriculo-ventricular opening, which is absent in the left. In this connection I may recall the fact, which one occasionally notices, of an amelioration of anginal symptoms when a degree of mitral insufficiency has established itself in cases manifesting cardiac pain, the distension of the left ventricle by residual blood being then less acute. I have, however, already pointed out that disease of the right heart may evince dextral angina.

Many theories have been advanced to account for the origination of cardiac pain. But inasmuch as the state is dependent upon many different anatomical conditions, no *one* theory suffices to

explain all cases. The causal factor may, as I have stated, be muscular, neural or hæmic in a preponderate degree, or a compound of these, and our duty is, so far as possible, to determine which of them plays the leading *rôle* in a given case, that we may direct our alleviative measures accordingly.

Taking the factors named *seriatim* as guides to treatment, what means do we possess for finding the key to the situation and for doing what is indicated? How can we best determine the predominant factor? How best use the key in a given case to provide a means of escape for the patient from a situation which, unrelieved, may quickly, or by recurrence, prove fatal? To give permanent relief may be beyond our power, but our responsibility ends with an intelligent endeavour to procure it. Fortunately, we have the power in a large number of cases to be of service.

The *muscular* factor may, as I have stated, be hypotrophic or hypertrophic in cases of cardiac pain. When the former, it is usually degenerated in fibre or weakened by fatty infiltration. Its weakness is generally manifested by the occurrence of cardiac pain on such moderate exertion as should not normally evoke it, and is probably due to a sudden rise of pressure within the chambers of the heart and its blood-vessels, associated in some case with an erratic contraction of a portion of its defective musculature.

Examination of the heart affords the usual signs of enfeebled muscular power, and of the vessels in a large number of cases, the evidence of increased arterial resistance. The age of such patients is usually past the meridian of life, and in a majority of cases they are men. Most cases of angina pectoris fall into this group.

The treatment of this, as of other varieties of cardiac pain in which relief is possible, divides itself into measures for immediate alleviation and into those for prophylaxis or prevention. The means selected for relief will vary with the degree of pain. If mild or moderate, the reduction of the work of the heart will be our first duty. This is usually, under these circumstances, easily accomplished by physical rest and vaso-dilators, of which the *nitrites* have deservedly the greatest reputation. Nitrite of amyl, trinitrine, or nitrite of sodium will usually accomplish all that is possible in vaso-dilation. The higher nitrates (erythrol tetranitrate and mannitol tetranitrate) may also be used.

When pain is more severe and these means prove insufficient morphia and atropine are indicated, and in this case the atropine is not added merely as a corrective to the action of morphia, but as tending to diminish the risks of syncope from pneumogastric inhibition under the stimulus of pain.

Still greater severity or persistence of pain demands a general anæsthetic—chloroform, ether, or a combination of alcohol with these. In any case it is essential that the physician should procure relief from pain before leaving his patient, even when the underlying condition is of a character to render recurrence probable or death inevitable. The inevitability of death cannot be determined *ante mortem*, but it may occasionally be *post mortem*, as in the case of right coronary thrombosis which I have mentioned, the vessel being suddenly and extensively obstructed, and the cardiac muscle pronouncedly degenerate.

The prophylaxis of cardiac pain in this variety implies the improvement of the tone of the cardiac muscle by attention to all the factors in the heart's action, by the avoidance of exposure to cold, or sudden calls upon the energy of the heart, either along the channel of the emotions or of physical or mental exertion.

This may appear to be a council of perfection, and as such be regarded rather askance by those who have had much experience of life, but the old proverb, which suggests the wisdom of endeavouring to procure a silk gown even if one is only likely to be successful in obtaining a sleeve of it, holds good under these circumstances, and is frequently rewarded by increased comfort and length of life for the patient.

With the practice of physiological righteousness in dietetic and other directions means may be taken to improve the cardiac tone by increased oxygenation of the blood, by muscular and neural stimulants of the cardiac muscle, and by the combination of these measures with less rapid and transient vaso-dilators than those used during the paroxysm of pain, such as the iodides and mercurials.

In arterio-sclerosis, without essential renal disease, the combination of *mercurials* with muscular and neural stimulants will be found of definite service. Although the reason for the necessary combination of these agents may not be quite

clear, empirically, the great value of such a combination is frequently demonstrated in practice.

When the muscular factor is hypertrophied in cases of cardiac pain, without being in any way degenerated, we have to deal, in the majority of cases, with aortic valvular disease, usually occurring in patients who are either young or below middle life. These are the cases which manifest what is sometimes called vaso-motor angina, and in which relief is temporarily obtained or hastened by the use of the nitrites. I say obtained or hastened, because, in any case, an accelerated action of the heart follows the inhibitory effect of the pain, which tends, by a succession of hypo-systolic contractions, to empty the heart and relieve its distress. Such anginous phases in the history of such a case usually coincide with a period of disturbed compensation, and subside with the recovery of that sufficiency of the heart's action which is termed "compensation."

When the heart, however, is greatly enlarged, and each systole, instead of falling in an intercostal space, delivers a shattering blow to one or more ribs, as may happen, an excited and erythetic condition of the cardiac muscle appears to be induced, which is associated with frequent attacks of cardiac pain, having all the characters of the so-called vaso-motor angina to which I have referred. The pain is relieved by the nitrites, but ever recurs, and then these agents appear gradually to lose their power and require to be repeated with increasing frequency. It is in such cases, among others of cardiac enlargement, that I for long thought that the therapeutic indication was an enlargement of the thorax by thoracostomy, to afford more easy play to the hypermyotic ventricle. I ultimately summoned up courage to put the theory to the test of experience, and published a case in the 'Lancet' of July 4th, 1908, in which this operation was performed at my request by my colleague, Mr. Ewen Stabb, with the happiest results. I show you photographs of the case, which declare the nature of the operation, and would refer those who desire further particulars of it to the source I have cited. I may add that the relief procured has proved permanent, as the patient now—a year after the operation—continues subjectively much more comfortable, although still suffering from occasional attacks of cardiac pain, for which he inhales with benefit a capsule of nitrite of amyl.

The *neural factor* is necessarily involved in all cases evincing pain, but there are instances and conditions in which it may legitimately be assigned a leading *rôle*, although always indissolubly associated with the muscular and hæmic factors, which renders the whole organic action a tripartite unity. As I have stated, the investigation of the cardiac nervous system in these cases has not been carried out with the care which it deserves, and which it will probably in time receive. I show you some interesting sections from a case of persistent angina pectoris, to which I have already referred, and which ultimately proved fatal, in which nerve elements may be seen in the wall of a coronary artery internal to the muscular coat, and which also revealed in the immediate neighbourhood of these nerve structures a minute intra-vascular aneurysm and general calcification of the coronary arteries. The cardiac muscle in this case, notwithstanding the diseased condition of the coronary artery, was on the whole well preserved. The attacks of pain were very frequent, and were relieved by the constant use of the nitrites, but an anodyne and stimulant, such as morphia and atropine, would probably have given relief for longer periods. It is now a good many years ago since this patient was under my care, when I was out-patient physician to the hospital, and these more powerful agents were not prescribed, as the patient could not be under continuous observation. But, when attacks are severe and frequent, and not associated with the powerful hypertrophied muscle I have described above, it will be found that opium in some form, as originally prescribed by Heberden and the older physicians, will afford greater and more lasting ease than the nitrites, which are transient in effect. Atropine as an adjuvant to opium is indicated, as I have said, both as an anti-inhibitant and as a cardiac accelerant like the nitrites.

But pain may, in every variety of angina, be so urgent, severe and persistent, that its relief may be imperative by more rapid and general anæsthetics. The late Dr. George Balfour highly recommended the use of these, even in cases which would scarcely come within the category of severity I have specified. The case of coronary thrombosis to which I have referred would, for example, have been a suitable one for a general anæsthetic, notwithstanding its degenerated muscle, because of the severity and persistence of the pain evinced.

These conditions, severity and persistence, in spite of the use of the nitrites and opium, naturally leave one no option but to send all our reserves into action, even though cardiac force may be weak. It is better that the last regiment should be engaged, even in a battle which will probably be lost, rather than that potential forces in aid should be left kicking their heels in idleness, as mere spectators of an impending catastrophe. They may, well-used and pushed home, snatch victory from the jaws of defeat.

We now come to a consideration of the therapeutic indications afforded by the third or hæmic factor in cardiac action, which raises many questions of ætiological interest, which it is not my purpose to discuss at present with any fulness. As I have said, all the factors in cardiac action are so intimately associated in the production of a common result—the action of the heart in health and in disease—that too exact a separation of them is apt to lead to more than their due share being attributed to each of them.

But the securing of a proper *quality* of blood, and the normal distribution of it when possible to the cardiac walls and within the chambers of the heart, is manifestly indicated in the presence of the symptom—pain, which from its character is calculated, like all pain, to disorder an organ which is beyond the power of the will, but very sensitive to the emotions.

A normal quality of blood being dependent upon its correct elaboration and the healthy action of the emunctories, demands treatment when defective, by the correction of the special error considered to be causal of the state in a given case. In connection with cardiac pain, or with pain simulating it, and in the absence of a recognisable cardiac lesion, likely to be primarily causal in its production, the blood may be in a condition of so-called anæmia or of so-called toxæmia, and in some instances both these terms may be applicable, and the hæmic may then be regarded as the leading ætiological factor. The former state (anæmia) is likely to occur in young subjects whose pains are "neuralgic," to use the only suitable but ambiguous term, and especially in women, who frequently evince thoracic pain not directly referable to the heart, intercostal in situation, and dependent upon stimulus originating elsewhere than in the heart—for example, in the stomach. We must be on our guard, however, not too hastily to come to this conclusion, for the "diagnosis" of dyspepsia has often, in the presence of dolor pectoris, been disastrous, both to the life of the patient and reputation of the physician. Assuming, however, a correct diagnosis, by the usual methods, of an anæmia, with pains cardiac or possibly so, the condition must be treated *secundem artem*, and in this connection pushing the use of arsenic carefully will be found very serviceable in this variety of cardiac pain.

The so-called toxæmic state, which appears frequently to be related, in some way not quite determined, to the defective excretion or metabolism of uric acid, is one which is also frequently associated with arterio-sclerosis and cardiac pain. It is in itself apparently causal of a measure of peripheral resistance by heightening arterial tonus in portions of the vascular system less involved in the chronic sclerotic process. It calls for treatment by the recognised diet and regimen. The wealthy, overfed and idle, might do worse than follow Abernethy's advice to such a patient, namely, to "Live on sixpence a day and earn it," with a little balneological treatment thrown in by way of consolation for their temporary and exemplary self-denial! "Poor man's gout" is usually a consequence of the excessive imbibition of malt and other alcoholic liquors, taken to enable him to cope with the excessive labour which is generally his lot, or to procure for him a transient exhilaration and oblivion in his struggle for existence. The treatment of this condition is educational and political rather than medicinal, although, in *statu anginoso*, the measures which are found to relieve Dives will also benefit Lazarus. A touch of colic "makes the whole world kin."

I need only further add in this connection, with reference to the treatment of cardiac pain, that certain imported toxic agents appear at times to induce it. Thus tobacco, used in excess, or where there is an intolerance of it, besides nauseating and diminishing the efficiency of cardiac pulsation, is found to be associated in some cases with this symptom. In such cases, which are not, in my experience, common, the removal, withdrawal, or abandonment of the agent apparently toxic must accompany any other measures taken for the relief of the pain.

The *quantity* of blood in the walls of the heart—

that is, the condition of the coronary circulation—is an important consideration in angina pectoris. By some it is regarded as the most important consideration. Huchard's last words on the subject are: "There are no anginas; there is but one—coronary angina—all the rest are false" ('Les Maladies de Cœur et leur Traitment,' 1908, p. 63). False or true, there is no question of the existence of pain due to cardiac conditions other than coronary arterial disease, and it is to cover all varieties that I have used, in this paper, the term "cardiac pain." But even in coronary cases the actual mechanism of the production of pain may apparently differ, and if this be so there must be varieties even in coronary angina. One meets, moreover, with apparently the same condition of coronary vessel, which in some cases is associated with pain, in others which have never been known to manifest this symptom. Edward Jenner, as we know, regarded calcification of the coronaries as a cause of angina, and his friend, John Hunter, died of it in association with such vessels. But we also know now that many cases of coronary calcification are never associated with this state. Complete occlusion of both coronary arteries by "a cretaceous clot which followed the principle divisions" of the vessels has been met with, unassociated with any cardiac symptoms (Rondeau, 'Bull. de la Soc. Anat.,' 1865, 2nd series, p. 253). It is specifically stated that during the ten days he was under observation this patient showed no cardiac signs and certainly no angina. He died of cancer of the liver, and is stated, prior to this illness, to have enjoyed good health. The muscular fibres of the heart were softened, icteric and "somewhat fatty." This case is also quoted by Dr. Samuel West in his remarks on the coronary circulation ('Trans. Path. Soc. Lond.,' vol. xxxv, p. 112).

Allan Burns was the first to suggest a century ago that a sudden deficiency of the coronary circulation underlay attacks of cardiac pain, and others have more recently described this state as "intermittent claudication," or sudden interruption to the circulation through a part, the blood-robbed muscle then developing conditions which originate the painful symptoms. The remarkable case of coronary thrombosis I have referred to would support such a theory were it not that coronary thrombosis, while known to be a cause of sudden death, as in the case of a youth, æt. 17 years, reported by Rolleston ('Brit. Med. Journ.,' 1896, November, p. 1566), need not necessarily be associated with angina pectoris. Sir William Church, however, published a case in which such occlusion was accompanied with cardiac pain and rapid death ('St. Bart's. Hosp. Reports,' vol. xxxii, p. 7). It was that of a man, æt. 40 years, who suffered from pneumonia complicated by infective endocarditis; the right coronary artery was "entirely obstructed by an embolism," whitish in colour, which the author suggests was probably detached from a recent vegetation on an aortic valve. Dr. Kanthack, who made the post-mortem examination, states that the coronary thrombus consisted of fibrin and blood and contained a few diplococci. The muscular fibres of the heart were apparently healthy.

In the record of this case it is stated that the patient had sudden præcordial pain and urgent dyspnœa at 3.15 p.m. on a certain date. This is stated to have subsided after a short time, and to have recurred an hour later more severely, and to be followed by death in a few minutes (p. 9). This would appear to suggest that a partial was followed by a more complete occlusion of the vessel, the pain in the first instance subsiding with the relief of pressure in the vessel, to be followed by more severe signs of the same kind on the establishment of permanent blockage. Quite recently (May 8th, 1909) Dr. Hugh Galt has published an account of "two remarkable cases of sudden death from unsuspected cardiac lesion" in the 'Lancet' (p. 1316), in which in the one case there was rupture of the right and in the other a similar lesion of the left coronary artery. Both these cases manifested as their only symptom epigastric pain.

There appears, therefore, to be some additional factor present, in coronary cases which manifest angina, besides the mere depletion of the cardiac muscle, and that factor I believe to be sensibility of the interior and walls of the vessel inself, which, in cases manifesting angina, is probably more accessible to stimulation.

Whether the condition provoking this sensibility be an aneurysm, a thrombus, an embolus of a particular kind or in a particular situation, a so-called intermittent claudication—a condition which is purely hypothetical—or a rupture of the arterial wall, the cardiac pain appears to be referable to sudden and sufficient intra-vascular pressure upon the probably sensitive end-arterium of the vessels

to suddenly raised intra-cardiac pressure within the chambers of the heart, or to laceration of the arterial wall, as in the cases quoted, as much as to defective or arrested nourishment of the cardiac muscle by depletion; in any case to a local impression made on the visceral nervous system in the first instance, however wide its subsequent referred radiation. Sir T. Clifford Allbutt's view of the aortic or aortitic origin of angina pectoris ('Lane Lectures Reprint,' p. 119) extended to the end-arterium of the coronaries and the endocardium itself, would seem to explain the persistent cardiac pain of such cases of sudden coronary blockage as I have referred to better than the assumption of some metabolic distress of the blood-robbed muscle, due to the interrupted current through it.

The lowering of this pressure in the coronary system is possible by a lowering of the general blood-pressure, and the more lasting freedom from pain in some cases may be owing to the absence of organic lesion other than a mere relative narrowing or inelasticity of vessels, which are, it may be, thickened in their inner coat, as is the case in all atheromatous conditions. The nitrites, therefore, as vaso-dilators, may be regarded as relieving pain by the general lowering of pressure which follows their use, and by the consequent freer irrigation of the heart with blood.

But the *quantity* of blood within the chambers of the heart also apparently plays a part in producing cardiac pain. And yet how many cases of cardiac dilatation do we meet with in which cardiac pain is absent? A dilating bladder beyond a certain point is painful. Beyond a still further point in dilatation the painful signs subside, and in a well over-distended and yielding bladder they may be almost or quite absent. Is, then, the surplus blood within the chambers of the heart a *consequence* or a *cause* of cardiac pain? Personally I feel disposed to consider that it may be both. The gradually distending heart, unlike the bladder or stomach, does not cause pain. The suddenly inhibited and distended heart is, however, associated with it under certain circumstances. The hæmic factor in such case would appear to be secondary to the neural, to which must be attributed the pain inducing inhibition of the heart, which gives rise to the distended ventricle, and it may be death in diastole, while the surplus blood in the chambers, may cause still further pain by pressure, until the residuum is removed. If such a case be auscultated during an access of pain, it will be found that the pulmonary second sound becomes accentuated, and as pain subsides this evidence of imperfect ventricular evacuation disappears. These signs are usually associated with an acceleration of the heart's action, which, by a quick succession of systoles, removes the residual ventricular blood, and this, again, coincides with the disappearance of pain. The nitrites, by flushing the periphery and accelerating the heart, thus aid the organ in its own effort to rid itself of the surplus blood in its chambers.

In this connection Dr. A. G. Auld makes an interesting observation in a lecture on "Asthma" published in the 'British Medical Journal,' for December 26th, 1908 (p. 1851), which not only shows the consequences of the action of the nitrites on the heart, but casts some light upon the mechanism of the production and relief of cardiac pain in certain cases.

"If the chest of a normal individual be observed through the screen," he writes, "and an inhalation of nitrite of amyl . . . given, it will be found in the course of two or three minutes that the chest expands and the lungs will be seen to flare up considerably. This added brightness lasts for a few minutes and then gradually subsides. Incidentally, it may be mentioned that if measurements be taken of the heart's shadow before and during the action of the drug it will be found that its transverse diameter diminishes considerably with the expansion of the lungs to the extent of one inch or even one and a half inches . . ." Thus, direct observation of the heart under the influence of this drug, which has deservedly a high reputation for relieving cardiac pain, precisely corresponds with the auscultatory evidence which accompanies the subsidence of angina pectoris. Thus, also, in cases in which hypertrophy is not great enough to cause the systolic heart to thrust injuriously against the resistant thorax, the nitrites diminish the bulk of the organ distended by residual ventricular blood; while, even in hypermyotic cases, which *do* injuriously strike the ribs and become erythetic in consequence, the same agent, by reducing in a measure the bulk of the organ in the manner suggested, tends to save it for a time from this injurious stimulation.

June 21st, 1909.

ACTION AND CONSERVATIVE VITAL REACTION, ESPECIALLY IN REGARD TO IDIOSYNCRASIES.

By F. PARKES WEBER, M.D., F.R.C.P.,
Physician to the German Hospital, London, and the Mount Vernon Hospital for Chest Diseases, Hampstead.

VITAL reactions, in the broadest sense of the term, include all those manifestations of irritability which distinguish living from non-living bodies. They generally (owing, doubtless, to a process of gradual natural selection) differ from non-vital reactions, *e. g.* ordinary chemical reactions, in being apparently useful (*i. e.* beneficial for the organism manifesting them), or "conservative" in nature, as if they were purposeful, as, indeed, voluntary reactions really are.

I would divide all vital reactions manifested in human beings into:

(1) Mental or voluntary nervous reactions.

(2) Reflex or involuntary nervous reactions.

(3) Vital reactions other than nervous reactions, whether manifested (*a*) by chemical changes, changes in temperature, etc., as in the production of antitoxins, or (*b*) by anatomical (macroscopic and microscopic) changes.

It is only the third class to which I shall here refer. Typical examples illustrating the conservative or compensatory tendency of such vital reactions are the following:

(1) The numerical increase of the polymorphonuclear leucocytes in the blood consequent on streptococcal infections, etc.

(2) Numerical increase of the red blood-cells connected with imperfect oxygenation of the blood and tissues in chronic cardiac and pulmonary diseases.

(3) The increase in size of skeletal muscles consequent on increased functional activity.

(4) Myocardial hypertrophy in conditions throwing abnormal work on a whole or a portion of the musculature of the heart.

(5) Thickening of the skin and subcutaneous tissue from intermittent pressure or friction.

(6) Hypertrophy of one kidney after removal or disease of the other kidney.

(7) The phenomena of the healing of a wound caused by chemical, physical, or mechanical agents with or without infective microbic complications.

In all such cases the "agent," whether chemical, physical, mechanical, or "functional," provoking the reaction and the conservative or compensatory nature of the reaction are obvious, but in some chronic infective diseases, such as tuberculosis, the process of cell-necrosis due to the "agent" (*e. g.* to the local presence of the tubercle bacillus) proceeds side by side in the infected animal with "reactive" attempts at local repair and limitation. Thus the *direct* effects of the "action" of the pathogenic "agent" (the tubercle bacillus in the particular instance in question) may be sometimes difficult to distinguish from the *indirect* effects of the infection, namely the results of the conservative vital "reaction," provoked by the action of the pathogenic agent. It is especially in chronic tuberculosis in adults, where the battle has been very slow and prolonged, that the anatomical results of morbid action are most intimately mingled with the conservative changes due to reaction. Undoubtedly many phenomena of disease, such as the fever in some infections, and the local inflammatory changes which occur in chronic tuberculosis and syphilis, are to be regarded not so much as direct effects of the pathogenic microbes (*i. e.* of the morbid "agents") and their toxins, as manifestations of the conservative vital reaction on the part of the infected organism. Naturally the scar-formation around chronic tuberculous or syphilitic lesions, the cicatrices left by boils and abscesses, etc., are to be explained in this way.

A person said to have an "idiosyncrasy" towards particular drugs or foods, such as eggs, certain shell-fish, beef, mutton, certain fruits, etc., or towards some physical "agent," such as heat and cold, is an individual whose organism "reacts" in a peculiar manner (unlike that of ordinary persons) towards the drug, food or physical agent in question. The idiosyncrasy may be the result of deficient or excessive force of reaction; it may be a peculiarity limited to a single member or shared by several members of the same family; it may be a congenital or acquired idiosyncrasy, temporary or permanent, and may persist unaltered or diminish with advancing age. Just as in normal persons repeated administration of small doses of some poisons (tobacco, opium, etc.) leads to the gradual establishment of a certain amount of tolerance ("mithridatism"), so also in individuals with idiosyncrasies towards special articles of food re-

peated administration of very minute quantities sometimes induces a certain amount of tolerance, especially after adult age has been reached. It has been suggested that the tolerance acquired in such cases is due to the formation within the individuals in question of an "anti-body," which renders them more or less "immune" to the food or substance which previously exerted a poisonous effect on them. Normal persons, without any such idiosyncrasy, would then have to be regarded as enjoying hereditary "immunity" towards all ordinary articles of food; in other words they would be individuals who possess all the requisite "anti-bodies" at birth or who gradually acquire them at normal intervals after birth. According to this view an individual, with an idiosyncrasy towards such articles of food as certain shellfish or eggs, is, as Dr. Hingston Fox has pointed out, an instance of reversion to an ancestral type of individual who lived under circumstances which precluded the use of shellfish or eggs as food. These articles of food apparently contain some principle which originally exerted a poisonous action on "normal" individuals. In the course of time, however, according to this view, a condition of tolerance became established in most persons; ultimately the majority (that is to say, "normal" individuals) came to possess such tolerance at birth or in early life (hereditary immunity), the individuals in whom such tolerance or immunity was defective being then regarded as abnormal, because they showed an "idiosyncrasy" towards the articles of food in question.

Probably the gradual diminution in effect of certain drugs, such as some purgatives, when persons employ them repeatedly (becoming "accustomed" to them), is to be explained, not as illustrating diminished force of "reaction" on the part of the individual organism towards the exciting "action" of the drug, but rather as illustrating the gradual acquisition on the part of the individual organism of a certain amount of immunity (tolerance—"mithridatism") in the manner just explained. If so, this would constitute a reason why persons who have to use purgatives should change the kind of purgative they use from time to time.

Roughly speaking, all drugs and therapeutic methods may be divided into (*a*) those whose beneficial effect may be explained as dependent on the vital reaction they provoke, and (*b*) those whose beneficial effect has to be otherwise accounted for (*e.g.* as being due to direct "action"). This classification appears to me to be very important, but it must not be forgotten that the same drug or therapeutic "agent" may exert quite different effects according to the dose employed. It is, of course, well known that many drugs, which (apart from idiosyncrasy) in ordinary doses exert a beneficial effect in special morbid states, may produce a contrary and harmful result when given in larger doses. The explanation, in my opinion, is that in the former case the beneficial effect results from the "reaction" on the part of the organism being more powerful than the direct "action" of the drug, whilst in the latter case the harmful effect is due to the direct action of the poisonous drug being prevalent, that is to say, overpowering the conservative vital reaction of the organism.* So in regard to the artificial production of toxic oligocythæmias and toxic polycythæmias, it appears almost certain that a toxin which in ordinary quantities will give rise to oligocythæmia, may in some individuals, when given repeatedly in very minute doses, give rise to polycythæmia. As an example of polycythæmia provoked as a "vital reaction" on the part of the organism towards a toxic agent we may cite the results of Belonovsky, of St. Petersburg, who claims to have increased both the number of corpuscles and the amount of hæmoglobin in the blood of anæmic persons by the injection of minute doses of hæmolytic serum. So also in regard to tuberculin, very minute amounts are said (in some individuals) to induce an increase instead of a decrease in the number of red blood-corpuscles. Doubtless, though much depends on the dose and duration of the action of the "agent" (that is to say, on whether single large doses or frequently repeated minute doses are employed), much must likewise depend on the condition of the individual organism, due to age, sex, habits, the quality of his bone-marrow, and the temporary state of his general health. Thus it seems reasonable to suppose that equal doses of a particular toxin when used in different individuals may give rise to oligocythæmia in some and polycythæmia in others, according to their body-weight, age, and temporary state of reactive power. The reactive power of the bone-marrow may, moreover, be affected by changes in its substance or in the blood-vessels which supply it with nutrient material and oxygen, and there are some persons who apparently differ from others in that their red corpuscles show a peculiar susceptibility (congenital or acquired) towards hæmolytic agents. Individual peculiarities of vital reaction may perhaps help to explain not only various puzzling phenomena of blood morphology in health and disease, but likewise many exceptional observations in regard to body-temperature and unusual clinical manifestations of various kinds.

June 21st, 1909.

* *Cf.* F. Parkes Weber, "A Note on Action and Reaction in Pathology and Therapeutics," 'St. Bartholomew's Hospital Reports,' London, 1903, vol. xxxix, p. 139.

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A CLINICAL LECTURE

ON

THE INTERPRETATION OF A TEMPERATURE CHART.

Delivered at St. Bartholomew's Hospital.

By NORMAN MOORE, M.D., F.R.C.P.,
Physician to the Hospital.

GENTLEMEN,—This boy forms the subject of my lecture to-day. I thought it would be worth while lecturing upon him, though his is not a very rare kind of case. Still, he conveys one or two important lessons in clinical medicine. He does not look particularly ill; he is past that period, and if I were to take his things off and percuss his chest you would not now be able to hear anything wrong at that distance. Close to, with the stethoscope, you would be able to make out that there is a very faint difference between the breathing sounds at one part of his right chest and those on the other side. It is a very faint difference indeed, so faint that I doubt whether anyone who had not watched it for several days would make it out. I have had the patient brought up because you will realise the patient better when you have seen him, even though there may not be very much that is morbid to be demonstrated.

This boy came into the hospital on September 28th. He was then in a feverish condition. He looked thinner than he does now, and the chief point about him was that he had a raised temperature; I show you the chart. At the end of September and the beginning of October you see that his daily temperature was over 101° F., that it sometimes rose to 102°, and it even reached 103°. It went on like that with a slight tendency to decline; it became a little lower, reached 99° F. instead of 100°, and did not go up as high as

103° any more. Still, this temperature chart lasted for more than a fortnight, and during that time we were naturally anxious about him. The point I wish to discuss with you is how you ascertain the meaning of such a temperature chart. And the first thing to remember is that it always has a meaning. It may seem shocking to us in a hospital where medicine is carried on accurately and systematically to think that there can be anybody going about who imagines that extreme variations of temperature are merely individual idiosyncrasies and have no morbid meaning. There are a great many people not medically educated who will tell you that, and I am sorry to say there are a few medical practitioners who sometimes, perhaps from overwork, drop into the frame of mind of thinking that there is some other way of accounting for a continued rise of temperature or a continually oscillating temperature than some definite morbid condition, and that they may, in fact, become inclined to think that they are dealing with a case of individual peculiarity. There is no such thing as an individual peculiarity upon that point. If a patient has a daily rise of temperature like this, what the old physicians would have called a "quotidian fever," there must be an explanation of it, some morbid condition which is going on in the body. In all the old books on medicine there is, of course, a chapter on fevers, and they begin by defining a fever. They said it was the natural heat of the body turned into something else, and they called these fevers "quartan," "tertian," and so on. Whenever you meet with a quotidian fever like this, or with any rise of temperature, you must try to explain it. Bring your medical knowledge to bear on the solution of that problem. If a child's temperature is raised for one day and then the rise disappears and he continues perfectly well, it may perhaps not be worth while to waste much time in deciding why it rose. Very often it would be quite impossible to do so. But wherever there is continued rise of temperature try to explain it; it is a matter of urgency that you should find out what the explanation is. During the first fortnight of this boy's stay in the hospital I felt unable to give a direct answer to that question. I considered several things, but I was not able to say which of them was the cause of the rise of temperature. Of course, at the present day, when there are so many helps to clinical medicine, one is anxious to make use of them all. And accordingly we had the Widal reaction tried several times. Not that this temperature is at all like that of enteric fever. But this temperature might have been that of enteric fever at the end of the second week and into the third week, if the patient had shown well-marked signs of disease in other directions—for instance, a distended abdomen, even if there were no spots upon it. This boy had not a distended abdomen, he had no spots, and his Widal reaction was invariably negative. So we had material for denying that he had enteric fever, and we did deny it: we were certain he had not. What other conditions were likely? Of course one listened to the boy's chest, and at one time a systolic murmur could be heard down the sternum and all over the front. It was not at all clear in sound, it could only be called a murmur if one rigidly adhered to the definition of a murmur, which is on the whole the best definition for clinical purposes, namely, that it is any addition to the normal sounds of the heart which is not a friction sound. There was an addition to the first sound in this case, but that ceased to be heard after a time. Had the boy ulcerative endocarditis? That temperature chart was consistent with it, and he might have had that disease. The murmur seemed rather to encourage the idea. But supposing there had been no murmur. He might still have had ulcerative endocarditis, because it is not an uncommon thing in that most serious, and I am afraid invariably fatal disease, to be unable to make out any abnormal heart-sounds for a long time. We sought next the help of the bacteriologists. It is a point in regard to which bacteriology is seldom able at present to give one very much help, though now and then it does. Nothing was found and no culture was made, so that we obtained no evidence of that disease from the bacteriologist. I still felt very anxious about the possibility of the boy having that disease, because, as I say, it is practically a mortal disease. On listening to the boy in the ward I expected sooner or later to hear very distinct cardiac murmurs, and I thought on the whole that that was the most likely explanation of his condition. But after a fortnight went by the boy's temperature began to decline, and instead of there being more murmurs, the murmur previously heard could not be made out, and no murmurs were audible; there was

now no alteration of normal heart-sounds. All this time—and this is a very important point—the boy was fairly cheerful, and mentally one did not notice much change from his ordinary demeanour. That was entirely against the supposition of his having enteric fever. I never saw a patient in the second or third week of enteric fever who could be said to be in the least like his natural condition. But I have seen patients with well-marked ulcerative endocarditis at all stages of the disease who were not depressed but quite cheerful, and who, considering they had such a mortal disease, were surprisingly little affected in themselves. So this absence of mental depression in this boy did not help us much; it was compatible with ulcerative endocarditis. Then the declining temperature was against the view that he had ulcerative endocarditis; it was not absolutely exclusive of it, however. You see I do not try to set the case out in tabular form, but to place before you what went on in my own mind with regard to the boy, because that is the way you have to follow such a case out in practice. The temperature began to decline, and at the same time the boy himself did seem a little better, if we can attach any importance to the general impression. In this fortnight, as I have said, there was a little difference in the breathing sounds on the two sides of the chest. Now let me tell you that when a patient is lying on his back in bed for a long time, you will often find slight physical signs in the lungs which do not mean that he is suffering from lung disease. He does not, under those circumstances, completely expand his lungs, and therefore there is less resonance in them; there is still more often rather less breathing to be heard in one part of the chest than in another. If it is not constant it is unimportant. In this patient we first of all heard on the left side a slight difference in breath-sounds from what we heard on the right. But it was quite clear to us when we listened two days afterwards that that difference had disappeared. A few days later it was clear that there was a little alteration on the right side, just about over the middle lobe of the right lung, and that alteration was constant. It was very slight, however, and I should have said it required a trained ear to discover it. A man who was just beginning auscultation would most likely not have noticed it. There was no bronchial breathing, and no crepitations were heard. What was discernible was a very fine friction sound. These are two notes which I made; one of them was a sort of farewell note to the idea of his having ulcerative endocarditis. "October 26th: no murmur audible, mixed râles on the right side, level of dorsal vertebræ 1, 2, 3. Heart's action much increased after coughing." It was very markedly increased after coughing. "October 29th: no râles. November 2nd: heart-sounds natural on the right back. At the base after coughing a sound as of a partial pleural adhesion was audible. No râles." What I mean by that is this, that where there is a strong adhesion between the pulmonary pleura, the outer surface of the lung and the parietal pleura, as the chest-wall moves you often hear a sound like a friction-sound. I do not know whether an adhesion was there, but it sounded more like the opening out of adhesions than like a regular rub of two surfaces one upon the other. That is a conjectural explanation, and it is perhaps only of use in conveying to you the kind of sound that was to be heard. That sound remained. So what it came to was this: that we did not count that sound as an established fact in his case until he had been in the hospital a month. He had a friction-sound at his right base which had been inaudible for a month, and he had a greatly raised temperature for a fortnight, a good deal raised in the third and slightly raised in the fourth week. Those were the positive signs which we had. And I think I ought to add to this the fact that the heart's action was very easily quickened, and at one time there was a very slight addition to the first sound of the heart. What diagnosis were those conditions compatible with? Let us take a diagnosis which is not a true diagnosis; at any rate, it is the accurate determination of a very important symptomatic condition: were they compatible with his having a right pleurisy? Had he some inflammation over some portion of his right pleura? They were, obviously. Even the heart conditions which he had might very well go with that. The heart conditions may, after all, have been changes not due to endocarditis; they were clearly not so. They did not last long enough, they were not definite enough; but when taken with the ease with which the heart was excitable they showed that some pulmonary condition had thrown an extra strain, probably on the right side of the heart, and so affected the whole of the

circulation through the heart for a time. So in that way they were compatible with pleurisy. The other symptoms were positive evidence of pleurisy —the friction-sound and the constancy of it. But could pleurisy account for all this rise of temperature? Was there something else in the case? It is clear that this temperature might be compatible with pleurisy. But as I said, pleurisy is merely the scientific name of a set of symptoms. When a man has a drawn and anxious expression and has a pain in his side, worse on drawing a breath, he is suffering from pleurisy. That is a very good definition. and it will seldom lead you wrong. And it brings you to the point that when you see a patient has pleurisy you have only taken the first step in the diagnosis. You have then to go on and say why he has pleurisy, and that will bring you to the true morbid condition which he is suffering from. So in this case, why had this boy pleurisy? Many people have pleurisy whom you see in the wards because they have had pneumonia; they have taken in the pneumococcus and allowed it to settle in the lung; it has consolidated the lung, and proceeded through the lung to the pleura, so that the patient has pleurisy. Pneumococcal pleurisy is common enough, but this boy had not pneumonia. He came in early in his disease and had no clinical history, which justified the belief that his disease began with pneumonia: What condition ought one to think of? There are a great many conditions which may lead to pleurisy and of which pleurisy may be the symptom. It is always well to think of the commonest things first, particularly in clinical medicine, and one of the commonest things is the presence of tubercle. Had this boy tubercle? Was tubercle the beginning of his pleurisy? Was the interference with the movement of the right lung and the pleurisy due to an invasion by the tubercle bacillus? He had no cough. How could you tell? He brought nothing up in which one could look for bacilli. A Calmette reaction was tried, but was negative. How could you tell? When you are acting for yourself never allow yourself to be forced to go against the facts. It is one of the unfortunate things about examinations, which are so useful in many other ways, that examiners have a habit of forcing candidates to express an opinion which is beyond the facts. It would very often be much wiser to say, "I prefer to be undecided on that point for another fort night." But, of course, for purposes of marking that might be a useless answer. If you were forced by the examiner to say what was the cause of the pleurisy, and you were to say tuberculosis, he would ask you, Why? You say because it is known to be on the whole the commonest cause of pleurisy occurring by itself in a boy of that age. You would be safe in saying that, because it would be supported by statistics. It is not a very strong form of opinion, because, although the thing is very common, it might be absent in the particular case before you. Yet I do not know any much better way of arriving at a conclusion with regard to such a case as this. It is perfectly clear that this temperature chart proves that some definite serious morbid change, most likely the development of some organism, was going on in the patient. It is clear from the later course that that organism did not flourish as it might have been thought likely to do at the beginning, but that its action gradually died down, and its effect ceased. Is that compatible with tubercle bacillus in the pleura? It is quite compatible. A very large proportion of the cases of pleurisy, whether there is a large quantity of liquid effusion in the pleura or not, especially in a boy of this age, are due to tubercle. So I think it highly probable; so probable that I should direct all my treatment on that line, that this boy had tuberculosis, the effect of which was pleurisy.

Let me point out to you what the difference is between that diagnosis and merely deciding that he had pleurisy. Supposing this boy had been knocked by a horse on the right side of his chest, or had any other severe blow of that kind, he might then have had local pleurisy. He then would most likely have had much more physical signs, but he would not have such a temperature chart. That points to the development of some morbid organism in the system, and that is the reason it deserves such very close attention and discussion. I brought this boy to consultation, and Dr. Fletcher suggested that it would be a good thing to have a skiagram done of him to see whether it showed anything. It was done, and showed some shadows in the chest, and it was suggested by the people who presided over the radiographic department that these were really the dark areas produced by enlarged glands, and that that was evidence of tuberculosis. Dr. Fletcher

suggested that we might very likely find something of that kind. I may mention that I am not myself convinced that those shadows do represent enlarged glands. If the boy had sufficiently enlarged glands to produce so much shadow, I should have thought that the signs of his tuberculosis, as exhibited in the temperature chart, would not have died down in the way they have. So we can say that he is, what he looks, perfectly well now.

The conclusion of what I have to say about him is this: always try to work out any febrile condition in that sort of way, until you arrive at a conclusion as to what is the morbid process which it represents. And the importance of doing that is that it is the only guide to your treatment. It is right to relieve the pain. This boy had hardly any pain, but if he had had pain in the side it would be right to relieve it, but no one would think he was thereby curing him of his pleurisy. The whole treatment must depend on your decision as to what the morbid process is. In a case like this we do the nearest best thing we can in the hospital. But if he were outside I should have that boy looked after as if he had had a most serious attack of the tubercle, even in his lung. If his friends ask, "Would you allow him to spend the winter at a high altitude instead of going back to school?" if it would not ruin his prospects I should say it was a very good thing. And if I were asked whether he should live in the country and have plenty of fresh air I should say "Certainly, it is of the highest importance." We shall send this boy to Swanley and do the best we can for him in that direction. But in every case in which you are able to arrive, as I have here, at a proper solution of the rise of temperature you will have done a great deal of good, because if these cases were recognised early as tubercular a great many lives would be saved. It is possible the boy still has a few lingering colonies of bacilli somewhere in his system, probably in his pleura, but not sufficient to keep the temperature up. What you want is to be certain as far as you can that all these colonies have died out. And the only way to do that is by giving him plenty of fresh air and abundant food.

June 28th, 1909.

WITH MR. BLAND-SUTTON AT MIDDLESEX HOSPITAL.

X.

The Natural History of Cancer of the Uterus.

On reviewing the facts relating to cancer of the various organs which we have considered in the preceding discourses, it was clearly set out that the leading features of this widespread and destructive disease are: its undoubted origin in epithelial cells, its insidiousness, its invasiveness, and its proneness to attack organs the seat of chronic disease. To these must be added the tendency of cancer to infect lymph-glands, and to disseminate, producing secondary growths in distant parts of the body, the massiveness of the secondary growths being often in striking contrast to the size of the primary cancer; the lethal effect of the disease is considerably retarded or accelerated according to the environment of the organ primarily affected.

A study of the natural history of cancer when it attacks the uterus is brimful of instruction in regard to these matters; and you will have ample opportunities of studying them, for patients with cancer of the uterus abound in this hospital.

In regard to the epithelial investment of the uterus, let me remind you that the endometrium of the cervical canal and the body of the uterus is lined with columnar epithelium, which is continued through the Fallopian tube to end at its cœlomic ostium, where there is an abrupt transition to the pavement-like epithelium (endothelium) of the peritoneum. The epithelium of the cervical endometrium undergoes a similar transformation at the external mouth (or *os*) of the uterus into the stratified or squamous-celled type, which lines the surface of the vaginal mucous membrane. The portion of the cervix uteri which projects into the vagina receives, by invagination, a covering of vaginal mucous membrane; the boundary line between the squamous cells belonging to the vaginal investment, and the columnar cells which clothe the walls of the cervical canal is situated, in a healthy woman, at the margin of the external os. It is necessary also to remind you that the epithelium of the uterus lines the glands of the endometrium, and, in the

case of the cavity of the uterus and the Fallopian tubes, the columnar cells are ciliated.

Cancer may attack any portion of this epithelial tract, from the squamous cells investing the vaginal portion of the neck of the uterus up to its termination at the peritoneal margin of the tubal ostium. The vulnerability of the epithelium so far as cancer is concerned varies very greatly in the various parts. Cancer in the cervical segment is dreadfully common, in the uterine cavity less frequent, and in the Fallopian tube rare. Its presence in the tubes was unknown, indeed, even unsuspected, before 1880. The relative liability of these three sections of the genital tract to primary cancer may be represented in this way. If the liability of the cervix be represented by five hundred, that of the body of the uterus would be twenty-five, and the Fallopian tube one. These comparisons are very striking even in the face of the fact that when cancer arises on the vaginal surface of the cervix, it is classed with those cases which arise in the epithelium of the cervical canal, whereas in the strict anatomical sense it belongs to the vagina. This is a matter which requires further notice because primary cancer of the vaginal mucous membrane is uncommon, or rare. Strictly, the vaginal mucous membrane ends at the margin of the os uteri, and cancer arising in the epithelial investment of that portion of the cervix uteri which is capped with squamous epithelium, should, as I have already remarked, be classed with vaginal cancers, but from the clinical point of view it would be an unpractical arrangement. Similarly, when cancer arises in the section of the vagina adjacent to the vulva, it will involve the vulval mucous membrane, and when well established it is difficult to determine whether it arose in the mucous membrane of the vulva or the vagina. Thus it comes about that, speaking generally, the only examples of cancer arising in the vaginal mucous membrane which run no risk of being classed as vulval, or uterine, are those originating in the middle segment of this mucous canal.

Cancer of the vagina is rare; for example, in the quinquennium 1904–8 three patients with cancer of the vagina died in the Middlesex Hospital. During the same period it is stated in 'The Eighth Report of the Cancer Research Laboratories' that 241 women with cancer of the neck of the uterus were admitted in the general wards and in the cancer asylum.

When we come to analyse the "social state" (as our registrars call it) of these women with cancer of the neck of the uterus, we find this disease especially common in women who have borne children, and disappointing as it may seem, fecundity increases their liability. Critical inquiry shows that injury (trauma) associated with coition and childbirth, but more particularly the latter, is a potent factor in producing the changes which render the epithelial tissues in this situation liable to cancer. This has already been pointed out in relation to primary cancer of the vulva (see Lecture IX). For ten years I devoted particular attention to this aspect of cancer of the cervix, and during the whole of that time whenever an example of this disease came under my notice in a woman, who had never been pregnant, I took unusual pains to satisfy myself that the morbid condition of the cervix was clearly cancer, and whenever possible a fragment of the affected tissue was removed and submitted to microscopical examination. In several instances the naked-eye diagnosis of cancer was discredited, the cancer-like tissue proved to be of the nature of granulation tissue in several instances, in a few it was exuberant glandular tissue, and in one tuberculous. One woman had such a suspicious condition of the cervix uteri, and though a microscopic examination of the growth left its nature in doubt, I advised the patient to submit to vaginal hysterectomy. The operation was carried out, and quite by accident she came under my care again after an interval of nine years for piles; she had remained in excellent health during the whole of that period. Many other examples of suspected cancer of the cervix which have remained free from recurrence after removal of the cervix or complete extirpation of the uterus come into this category. On one occasion a harlot, æt. 25 years, came under my observation with a lesion of the cervix which appeared to be cancerous; all who saw it were satisfied that the lesion was malignant. I was not so sure about it; the age of the patient, and the fact that she had never conceived weighed in my mind against cancer, so instead of removing the uterus I cut off the vaginal portion of the cervix and divided it into three pieces; I bestowed a piece on two competent histologists and kept one myself for examination. The histologists decided that the disease was cancerous. Although I remained doubtful I totally removed the uterus.

Five years later the patient reported herself in excellent health. Reflecting on such experiences, I cannot help coming to the conclusion that where there is diagnostic doubt the disease is set down as cancer when it is really inflammatory or of infective origin. If every case reported as cancer of the neck of the uterus which occurs in virgin-spinsters is submitted to rigorous diagnostic tests, supported by a careful microsopic examination of the tissue, I feel sure that these patients will only form about 1 per cent. of the total.

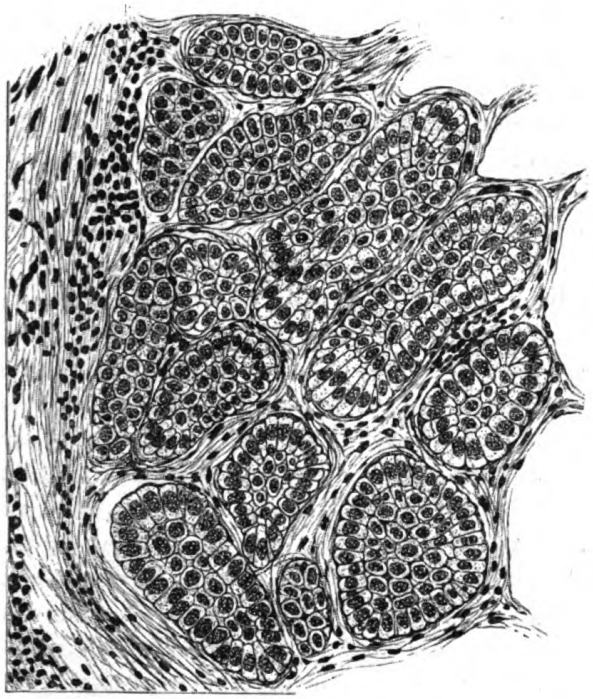

FIG. 1.—The microscopic characters of cancer arising in the neck of the uterus.

In dealing with cancer of the vulva (Lecture IX) mention was made of the leucoplakic condition often seen on the inner surface of the labia and of its significance as a precursor of cancer. A similar change is sometimes seen on the neck of the uterus; I have observed it, but the common morbid condition which not only precedes cancer of the neck of the uterus, but which when severe is often mistaken for it, is the morbid condition which used to be called ulceration of the cervix, or erosion, until Ruge and Veit (1878) showed that the soft pink tissue was not due to ulceration, but consists of an overgrowth of the glandular tissue of the cervical canal which over-runs the cervix uteri around its "os." A common sequel to childbirth is laceration of the neck of the uterus, and in multiparous women it is often disfigured by fissures radiating in various directions from the os, and in the recesses of these fissures you will find collections of this strawberry-pink tissue. The opinion is strongly held by many thoughtful men that these fissures, and especially the glandular tissue connected with it, constitute a pre-cancerous condition. The changes are often termed cervicitis for clinical convenience, and recent investigations on the early stages of cancer arising in the cervix uteri unanimously support the views that cervicitis and glandular changes are pre-existent in all cases. The

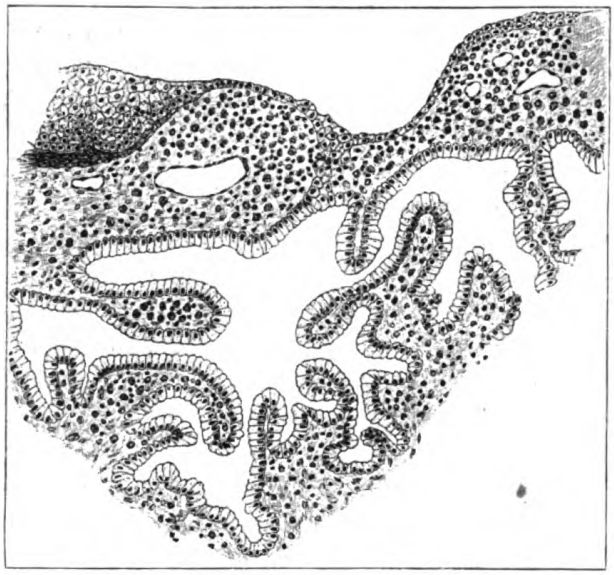

FIG. 2.—The microscopical features of the pink tissue at the neck of the uterus commonly called "an erosion." (After Bonney.)

precise cause of these chronic changes has not been identified, but it must be something peculiar; certainly the history of women who come under observation with long-retained pessaries show that something more than long-continued irritation, ulceration and dirt is necessary for the production of cancer in the neck of the uterus. It is also a fact that women are occasionally brought to us in consultation under the impression that they are suffering from advanced cancer of the uterus, and on examination a forgotten pessary is discovered. A remarkable case of this kind happened to me in 1908. A Jewess, æt. 65 years, and diabetic, had a carcinoma in her right breast. Arrangements were made for its removal, and on the morning of the operation the nurse told me that the patient

had a foul vaginal discharge. The doctor thought it might be due to uterine cancer secondary to the disease in the breast. I expressed the opinion that it probably depended on a forgotten pessary. I removed the breast and dressed it carefully, and then examined the vagina and extracted a vulcanite pessary. The stench may be imagined, but it was indescribable. Later we ascertained that it had been in the vagina certainly twenty-seven years; the patient assured us that she would never allow anyone to remove it. It is true that Dr. F. J. McCann has observed an example of primary cancer of the vagina associated with a pessary. A woman, æt. 70 years, had worn a ring pessary for four years without removing it. When she came under observation a ring-shaped cancerous growth was found in that portion of the vaginal mucous membrane which came in contact with the pessary. No one has attributed any malicious influence to vaginal pessaries so far as cancer is concerned. As has been mentioned already, cancer of the vagina is rare but the use of pessaries extremely common. In 1902 I attempted to collect some statistics in regard to pessaries. One London maker stated that he supplied ten thousand rubber rings and globular pessaries, and three thousand vulcanite "Hodges" annually. Another supplied the trade with thirty-six thousand yearly, and added, "vast quantities of pessaries are imported from Germany and other countries." There are several makers of pessaries in London, so that you will be able to form some notion concerning the frequency with which they are employed. Though the persistent use of a pessary is not favourable to cleanliness, it cannot be charged with causing cancer.

Cancer of the body of the uterus.—The consideration of cancer arising in the epithelium lining the cavity of the uterus proper proves that the social state of the patient plays here a part as conspicuous as in the case of the cervix. At first sight it may seem to you somewhat arbitrary to divide uterine cancer into two classes according to its situation in the neck, or in the body of the organ, but this arrangement is well justified. It is undeniable that cancer may arise in the uterine epithelium at any point from the external os to the fundus uteri; it is, nevertheless, uncommon to find a primary cancer in the endometrium of that part of the canal which traverses what is well known as the supra-vaginal section of the cervix uteri; when it arises in this section it is a very insidious and treacherous form of the disease. The remarkable feature in regard to cancer when it arises in the epithelium of the corporeal endothelium, or, as it is termed in clinical phraseology, "cancer of the body of the uterus," is the reverse of the conditions surrounding its ætiology when it affects the neck of this organ, for it is more common in virgin-spinsters and barren married women than in mothers.

Our knowledge of cancer of the corporeal endometrium is of fairly recent date. Twenty years ago it was regarded as an uncommon disease, but since hysterectomy as a radical method of treating obstinate uterine disease has come to be more freely and safely practised, we have acquired some accurate knowledge in consequence. This new knowledge has served to establish the fact that cancer in this situation is more frequent in childless women and aged spinsters than in fertile women; it also shows that it is commoner at the menopause than at any other period, whereas cancer of the cervix is especially common between the fortieth and fiftieth years of life. Accurate pathological investigations of the corporeal endometrium have shown that there are some epithelial perversions in this tissue which mimic very closely cancerous formations, except in the all-important particular that they are not malignant. To my mind the most noteworthy observations in this field are those of Piquand. In 1905 he drew attention to the frequency with which a submucous fibroid was associated with cancer of the corporeal endometrium, especially in women of fifty years and upwards. In this connection he also emphasised what other observers had pointed out, namely, that a submucous fibroid is usually associated with changes in the endometrium, which not only cause excessive bleeding, but set up inflammatory changes giving rise to leucorrhœa, salpingitis, pyosalpinx, and such changes in the epithelium as render it susceptible to cancer. Piquand's statistics support his views. I have examined my own cases in the light of his statements, and the result may be briefly expressed in this way: That among women submitted to hysterectomy for fibroids over the age of fifty years, about 10 per cent. of them will have cancer of the corporeal endometrium. Kelly and Cullen, among 1674 cases of hysterectomy for fibroids, found twenty-three examples of carcinoma of the body of the uterus. If these con-

clusions are confirmed by other observers, the suspicion that submucous fibroids predispose to cancer will be transformed into a grim reality, and warn practitioners of the dangers of allowing the disease to drift into an inoperable condition simply because the patient has attained the age of the menopause. There is another perversion of the uterine epithelium often overlooked in less pronounced examples, whilst in extreme cases it is apt to be mistaken for cancer of the body of the uterus, namely, the morbid condition known as diffuse adenomyoma of the uterus. Indeed, there is reason to believe that exceptionally it terminates in cancer. From a careful examination of some specimens described as adeno-carcinoma of the body of the uterus, I have come to the opinion that some cases so described were really examples of diffuse adenomyoma. This disease, like cancer, may arise even in small, atrophic uteri (Fig. 3).

An interesting feature of this disease is the frequency with which uteri attacked by it show traces of antecedent inflammation, for not only are the Fallopian tubes frequently thickened and their cœlomic ostia occluded, but the uterus itself is often firmly adherent to the bladder, rectum, intestines and adjacent peritoneum. Diffuse adenomyoma not only simulates the symptoms and physical signs of cancer of the body of the uterus, but it may be in itself a pre-cancerous condition.

Concerning the early stages of uterine cancer we know little, but we know more of the beginnings of this disease in the neck than in the body of the organ. A careful and regular attendance at a gynæcological clinique in any large British city or town will soon satisfy an observant student that cancer of the cervix uteri begins in a fissure left by the healing of a laceration following child-birth, or as a circular ulcer with raised edges, or in an exuberant papillomatous form. The ulcerating type is common, the exuberant form rare. The mode in which the disease begins in the cervix is a parallel of its beginnings on the edge of the lower lip. So far as the early stages of cancer arising in the corporeal endometrium are concerned, very little derived from actual observation is forthcoming, but what we know of the disease when well advanced is sufficient to enable me to tell you that there is an ulcerating and there is an exuberant or massive form. In regard to these I shall have something to say later, but let me here state that on two occasions only has it fallen to my lot to see primary cancer of the corporeal endometrium in such an early stage that the disease was limited to the superficial layers of the endometrium.

In all parts of the body there is often great difficulty in determining from a clinical examination whether in a given case the patient is suffering from cancer, a simple tumour, or an inflammatory swelling; moreover, the employment of the microscope will not always decide. There is no certain sign of cancer. The uterus is no exception to this rule, as the following case serves to show: A multipara, æt. 83 years, complained of uterine bleeding,

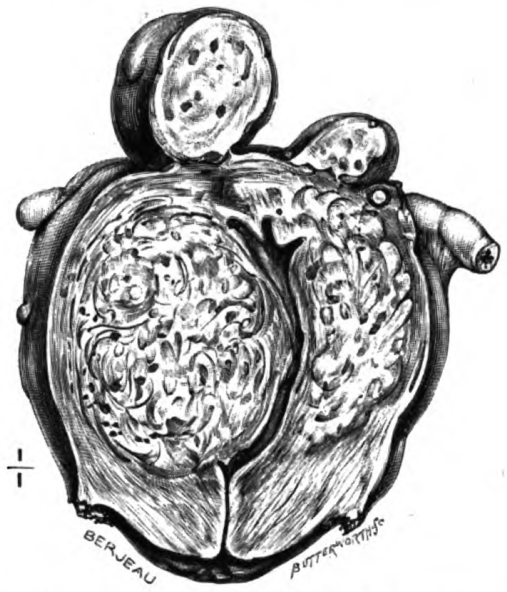

FIG. 3.—A small uterus with diffuse adenomyoma from a barren married woman. The uterus is represented in coronal section.

for which she was examined under an anæsthetic; fragments from the uterine cavity were secured by a curette, and after a careful microscopic examination were pronounced to be cancerous. The age of the patient was held to be a bar to hysterectomy. She came under my care; as the old lady appeared to be otherwise in good health I decided to remove the uterus. Vaginal hysterectomy was performed, and on examining the soft growth which filled the uterine cavity I found that it resembled in every particular the villous papillomata so common in the urinary bladder (Fig. 4). This view of the microscopic characters of the growth was confirmed by a committee of the Obstetrical Society, which critically examined and reported on

the specimen (see 'Trans. Obstet. Soc., London,' vol. xlix, pp. 46, 93). The correctness of this opinion is supported by the fact that three years after the operation the patient was said to be in good health (April, 1909).

Let me also draw your attention strongly to the fact that cancer of the body of the uterus occurs in aged spinsters and barren wives, women in whom the uterus after the forty-fifth year is below the average size, unless it happens to contain fibroids. After the menopause the uterus in such women rapidly shrinks, and becomes a small atrophic organ.

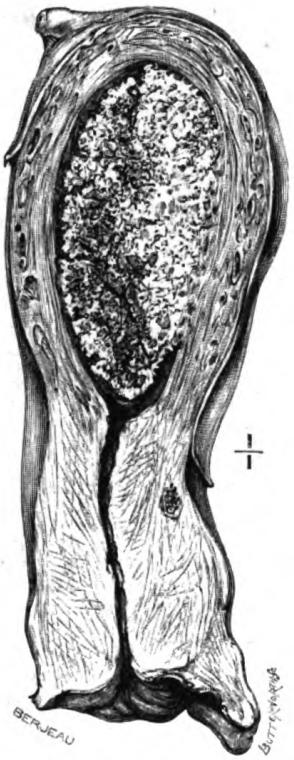

FIG. 4.—A uterus with villous disease of the endometrium. Removed from a multipara, æt. 83 years.

The corporeal endometrium of such an atrophic uterus occasionally becomes the seat of cancer, and it is very likely to be overlooked, and this for two reasons: the chief one is due to the fact that the vagina is so extremely narrow that it prevents an adequate examination, and in patients in whom it can be carried out the uterus is found to be so small that the possibility of cancer being present is not entertained.

I want to impress on your minds very carefully that the size of a uterus is no guide in the diagnosis of cancer of the corporeal endometrium; I have found a uterus cancerous when the whole organ scarcely exceeded the dimensions of a man's thumb, and I have seen one so stuffed with cancer that it reached the navel. Observation teaches that cancer of the corporeal endometrium of an atrophic uterus is of a low degree of malignancy.

Variations in malignancy.—There is a clinical feature of uterine cancer whether it attacks the neck or the body of the organ which is not thoroughly appreciated: I refer to variations in its malignancy. We do not sufficiently realise that cancer may arise in the uterus and destroy the patient's life in twelve months. Many untreated cases run on for two, three, and even four years, and in the case of the body of the uterus for much longer periods. Cancer, it is true, varies widely in its malignancy in nearly all the situations in which it grows. Cancer of the breast in a suckling woman will run its deadly course in a few months, but in an older woman it may require ten, twelve, and even twenty years to destroy the patient. Cancer of the cæcum will in exceptional cases grow so slowly as to require five, and even seven years, to kill its victim, and the same is true of cancer of the rectum.

Cancer and sepsis.—As a rule, cancer of the neck of the uterus runs its course more rapidly than the same disease inside the uterus, but this is due to an accidental circumstance, namely, the rapidity with which a cancerous cervix becomes septic. This is a matter of great importance.

An innocent differs from a malignant tumour in the possession of an investing capsule, and as long as it remains intact the tumour is protected from pathogenic micro-organisms. When the capsule is injured or sloughs infecting agents gain access to the tumour-tissue, causing general disturbance of the patient's health. Cancer possesses no capsule, and as a rule is situated on epithelial surfaces where it is exposed to micro-organisms, for example, the lips, the gullet, tongue, larynx, stomach, intestines and cutaneous surfaces. The exuberant tissue formed by the growth of the cancer being poor in blood-vessels, and therefore of low vitality, is easily infected by pathogenic micro-organisms and decomposes: the products of these changes are cast off as offensive discharges, the infective agents gain access to the blood-stream, set up general disturbance of the patient's health, and produce the peculiar sallow complexion which used to be termed the "cancerous cachexia," but

which is in reality due to the absorption of the products—toxins—brewed by the micro-organisms.

In the case of cancer of the tongue this condition of things is so well recognised that surgeons, in preparing patients for removal of a cancerous tongue, knowing full well the dangers they run from sepsis due to swallowing, as well as the inhalation of the germ-laden and toxic-containing discharges from the ulcerated surface, do their best to render the individual immune by vaccinating him with a prophylactic serum.

It is noteworthy that, as a rule, those cancers run the most rapid course which are situated in positions most accessible to pathogenic micro-organisms. The tongue and larynx are good examples, but probably in no other situation in the body can this be so strikingly demonstrated as in the uterus. Cancer in the cervix becomes septic more rapidly than cancer within the uterus, and the modes by which this disease destroys life in these two situation differ in some very important particulars. Before proceeding to discuss these points it is also necessary to remind you that cancer of the same organ shows marked differences in malignancy in different individuals as I have already mentioned.

Until menstruation is established the vagina and the uterine cavity are to be regarded as functionless canals, and in virgins they are practically air-tight. After marriage and child-birth, air, and therefore micro-organisms, obtain access to the vaginal passage and the vaginal portion of the uterine cervix; consequently when the cervix is attacked by cancer, the morbid tissue is as liable to decompose as when cancer attacks the tongue. It is the accession of septic changes in this cancerous tissue which causes cancer of the neck of the uterus to be such a distressing disease, for as the ulceration extends to, and opens up adjacent viscera, such as the bladder and the rectum, it also involves the ureters, leading to septic infections of the whole urinary tract. The extensive ulceration and sloughing of uterine, vaginal and rectal tissue which is such a well-known feature of this disease is greatly promoted by the septic infection. Indeed, it may be stated that the death of patients affected with cancer of the uterus is mainly brought about by sepsis. Chief among these terminal infections are uræmia and peritonitis, the latter being due to perforation of the wall, or actual leakage of purulent fluid from the Fallopian tubes, which become distended with infective fluid, secondary to the accumulation of septic material in the uterine cavity. In a small proportion of cases, probably 6 per cent., the uterus is in the condition known as pyometra, and in exceptional instances the septic fluid pent up in the uterine cavity leaks through a hole caused by ulceration in the uterine wall. Thrombosis of the iliac veins is not uncommon, and its sequelæ, gangrene and pulmonary embolism. Uræmia is the most frequent of all the terminal infections which occur in women with cancer of the cervix uteri; it is due to the implication of the vesical segments of the ureters and the bladder. Those who have carefully carried out systematic examinations of patients who have died from cancer of the cervix uteri draw attention to the frequency with which dilatation of the ureters and the renal pelves is found. Indeed, some observers fix the frequency of ureteral and renal complications in this disease as high as 70 per cent.

Without accepting this high proportion of renal complications, no one who has had opportunities of following cases of cancer of the cervix to their termination can doubt that uræmic symptoms are present in the majority of these patients. (It may be mentioned here that cancer of the rectum in women and men frequently destroys its victims by uræmia and anuria, caused by the bladder and the ureters being implicated by the cancer.) This unhappy picture does not end here; it is the presence of septic micro-organisms in this cancerous tissue which makes the efforts of the surgeon approach in some measure to the labour of Sisyphus. If you study carefully the results of the earnest and praiseworthy efforts now being made to relieve, by surgical means, women suffering from cancer of the neck of the uterus, you will find that it is not the technical difficulties which baffle the surgeons, it is the difficulty of controlling the sepsis; it is this which accounts for the high mortality of what is known as the radical operation for cancer of the cervix, and among the various micro-organisms which lurk in cancerous tissues the virulent streptococcus is frequently found. It is true that most surgeons, as a preliminary to such operations, remove by scraping and cauterising the redundant and infected tissue, but it is time they followed the practice mentioned in regard to the treatment of cancerous tongues, and attempt to control these

micro-organisms by a vaccine before resorting to hysterectomy.

Another feature which cancer of the neck of the uterus shares with cancer of the tongue is the infrequency of secondary deposits. Dissemination of cancer is a slow process, and in those situations where this disease kills comparatively quickly as a consequence of septic complication, secondary deposits are few in number, small in size, and only obvious in a small proportion of cases. In cancer of the tongue the adjacent lymph-glands quickly

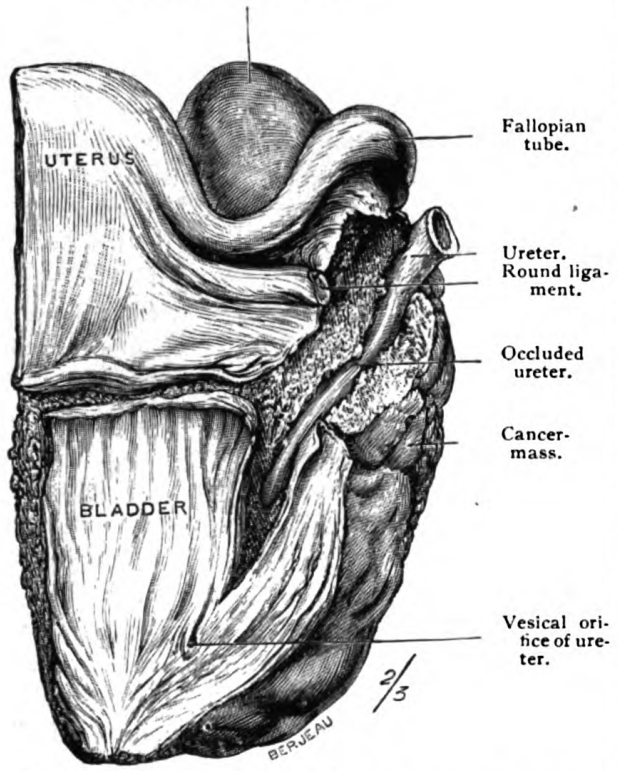

FIG. 5.—Cancer of the neck of the uterus implicating the ureter.

enlarge; this is not the case in cancer of the cervix, indeed, some careful investigations show that in the bodies of patients in whom the disease has run its fatal course, enlarged lymph-glands are found in about half the cases, and it is a fair computation that among the women who are submitted to hysterectomy for cancer of the uterus, in about one third of the number the lymph-glands in the pelvic and lumbar regions will be enlarged. It is important also to remember that because a pelvic lymph-gland is enlarged in a patient with cervical cancer it must not be assumed that the increase in size is due to cancerous infection. A careful microscopic examination will often prove that it is due to inflammatory changes. It cannot be too strongly impressed on your minds that there is no certain means of determining clinically whether an enlarged lymph-gland is cancerous or not without a microscopic examination. Hardness is no test; a very soft gland may be full of cancer-cells, and this is a matter of some practical importance, because in removing lymph-glands stuffed with cancer-cells, especially if they be roughly handled, the capsules of the glands will break, and the cells escape and lodge in the connective-tissue surfaces exposed during the manipulations; these cells grow and form new masses of cancer. This is known as "cancer infection"; I have often drawn attention to its occurrence after extensive operations for cancer, and it is a frequent cause of failure (see especially Lecture III), and it is a noteworthy fact, to which Comyns Berkeley has recently drawn attention, that in cases of radical hysterectomy for cancer of the neck of the uterus, where the removal of enlarged lymph-glands forms a prominent feature of the operation, quick recurrence is the rule.

A comparison of the course of cancer arising inside the uterus, with that of cancer originating in the cervix, will serve to illustrate the part played by pathogenic organisms in shortening the duration of the disease. It has already been mentioned that the uterine cavity in virgin-spinsters and barren women is practically an air-tight chamber, and that cancer of the corporeal endometrium is more prone to arise in sterile women than in those who are fertile. When cancer arises in the body of the uterus of a multiparous woman—a rare occurrence—the cervical canal is patent and occasionally septic. In such an event the disease assumes the form of a destructive cancerous ulcer, such as we are familar with in the cervix. When cancer arises in the corporeal endometrium of a barren uterus with a narrow cervical canal it assumes the massive form. Take, for instance, the specimen represented in Fig. 6: the uterus is enlarged to nearly thrice its ordinary size; its cavity contains an unencapsuled mass of cancerous tissue; its walls are thin, due to the slow expanding force exercised by the persistent growing mass within. If you examine the specimen critically, an outrunner from the cancerous mass will be seen creeping down the cervical canal, and the tip of it emerges through the mouth of the womb as a slough. This uterus was removed from a spinster, æt. 56 years, on account of irregular hæmorrhages.

It is clear from an examination of the specimen that the cancerous mass had been growing within the uterus without causing symptoms until the tongue-like piece of growth protruding from the os uteri became septic; then she became conscious of bleeding, and this eventually led to the detection of the disease within the uterus.

Some of you may ask, and with reason, what changes would have happened in the uterus had the disease remained undetected? This is not difficult to answer. I have already mentioned that when pathogenic micro-organisms invade cancerous masses they cause it to decompose and slough (the fragments escaping with the fœtid discharges which constitute such a disagreeable and often disgusting feature of the late stages of uterine cancer). The patient thus becomes exhausted by a combination

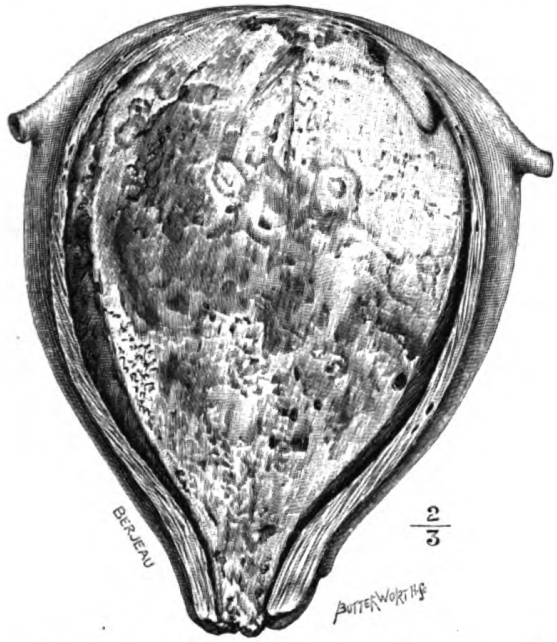

FIG. 6.—A cancerous uterus in coronal section. The cancer is of the massive kind. From a spinster, æt. 56 years.

of general septic infection and recurrent uterine hæmorrhages. There is another way in which cancer of the corporeal endometrium causes death. Cancer-cells possess the dangerous property of eroding tissues with which they are in contact. This invasiveness of cancer-cells in the case of the uterus leads them to permeate and penetrate its muscular walls, and the cells escaping into the belly engraft themselves on the walls of any organs, such as intestine, ovary, or omentum, which may happen to be in its vicinity. In some cases the cancerous process may appear as a small "bud" on the serous surface of the uterus. In the woman from whom the uterus and bladder represented in Fig. 7 were taken, the peritoneal investment of the abdominal viscera presented minute cancerous nodules in thousands. Rarely the cancerous mass may form a boss on the fundus of the uterus as big as a golf-ball (Fig. 8).

I am anxious to impress upon you in regard to this matter an important fact; it is this: A primary cancer of the body of the uterus may completely permeate the muscular tissue of the fundus and fail to produce any irregularity in the contour of its serous surface, but in spite of this the general peritoneal cavity may be seriously infected. I performed hysterectomy on a spinster, æt. 60 years, on account of menorrhagia, which was attributed to a submucous fibroid. The uterus was removed, and before closing the abdominal incision I looked carefully around, and caught sight of a flattened

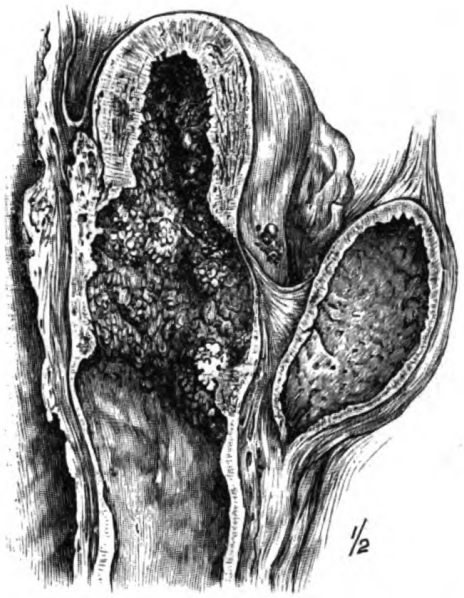

FIG. 7.—Cancerous uterus in sagittal section. A bud-like process of cancer has eroded the uterine wall and protrudes on the peritoneal surface. The peritoneum was dotted with thousands of secondary nodules.

discoid mass, 10 cm. in diameter, lying in the great omentum; it was removed. This mass and the uterus were hardened, and two weeks later the omental tumour was examined microscopically and found to be a secondary deposit of cancer. I at once bisected the uterus, and found that it contained a submucous fibroid, and the uterine cavity contained a quantity of soft cancerous material. We at once realised that the cancer had become extensively generalised in the belly to produce such a large lump in the omentum, and that the outlook for the patient was bad. She died with extensive abdominal recurrence four months after the operation. This case shows well what an insidious process cancerous permeation is—slow, persistent, and painless. In this case there was nothing on the peritoneal aspect of the uterus, and

nothing to be seen on the pelvic peritoneum, and no enlargement of the pelvic and lumbar lymph-glands to lead me to suspect that the peritoneum was thoroughly infected with cancer-cells. The only symptom of which the patient complained was irregular losses of blood from the vagina, and the only physical sign was an enlargement of the body of the uterus. Pain and tenderness were absent.

You should remember these facts, because you will from time to time hear a gynæcologist exclaim on examining a woman with advanced cancer of the uterus: "What a pity you did not seek my aid earlier!" Do not imitate this. You will unfortunately see many similar cases when you practise the art of gynæcology. Do not upbraid the patient; she has no idea when she consults a doctor that her uterus is cancerous, and even when such women come for advice in the early and doubtful stages, the practitioners lack the courage to advise a serious operation when diagnosis is uncertain.

FIG. 8.—A uterus in sagittal section. The endometrium is cancerous, and the disease has involved the muscular tissue and formed a large knob on the fundus of the organ.

The idea of instructing women by issuing pamphlets concerning the early stages of uterine cancer is to fill their minds with fear. It seems to me that a propaganda of this kind only serves to add another terror to the life of suffering woman.

June 28th, 1909.

ON THE TREATMENT AND PROGNOSIS OF CASES OF HIGH ARTERIAL BLOOD-PRESSURE.

By O. K. WILLIAMSON, M.A., M.D., B.C.Cantab., F.R.C.P.Lond.,

Physician to Out-patients at the City of London Hospital for Diseases of the Chest, Victoria Park; Assistant Physician to the East London Hospital for Children.

IT is important that the practitioner should recognise the fact that if cases of high arterial blood-pressure are to derive lasting benefit from his treatment he must deal with them in the early stage, that is, before the advent of permanent arterial and cardiac changes. For it is only thus that he can hope to prevent the inevitable result of these conditions, which, broadly speaking, is death either from heart failure or as the result of cerebral hæmorrhage.

It is unfortunately too frequently the physician's fate to see these patients for the first time only when the condition is an advanced one, and when the most which he can hope for is to be able to delay somewhat the final catastrophe.

Granting that we are face to face with a case of extremely high blood-pressure, the question at once presents itself not only how far we can but how far we ought to attempt to reduce the pressure.

It is probable that no general rule can be laid down, but that the treatment most suitable for a particular case must be determined by careful trial, noting the effect of apressor (those which reduce blood-pressure) remedies on the general condition of the patient.

It would seem, however, that if there be one point more than another which requires particular attention it is the effect of such treatment on the renal circulation as evidenced by the urinary excretion, and it is perhaps a sound general rule that we should not reduce the blood-pressure to such a degree as to cause diminution in the daily amount of urinary solids excreted.

The following remarks, which deal with advanced cases under my care, whilst not in any way pretending to embody a complete account of treatment in these conditions, yet may, I would hope, supply some practical hints.

The method which I have usually adopted with these hospital patients has been to give no drugs other than simple aperients for a few days or a week so as to note the effect of rest in bed, and thereafter to order the patient or to remove from him one drug at a time. It is only thus that we can hope to learn the effect of a particular drug. The same method has been employed in regard to other methods of treatment such as diet or exercise. Thus to take a concrete case. A patient is at rest in bed for a week without any alteration in blood-pressure resulting. He is then given a drug, say potassium iodide, with no other alteration in treatment. Any change in blood-pressure which follows may fairly be ascribed to the remedy. Let us further assume that the pressure after an initial fall remains constant for another week, and that at the end of that time we allow the patient to get up for a certain time daily. A change in the blood-pressure following this may then be ascribed to the cessation of confinement to bed.

In the records detailed below the drug treatment is noted in every case, together with the changes in this, and as far as possible, all other circumstances (such as alterations in diet) which may affect the blood-pressure.

The instruments used were either Stanton's blood-pressure instrument or Oliver's compressed air hæmomanometer, both modifications of the Riva-Rocci method. These instruments give identical readings. When there is no statement to the contrary the patients were observed in the recumbent posture in bed and the observations made on the arm. Only results of systolic pressure* are given.

The results are recorded in millimetres of mercury (mm.).

No. 1.—C. H—, female, æt. 44 years. Arterio-sclerosis with dilated aorta. Admitted to hospital April 19th, 1907. Up till the time of the first observation on April 25th she was on no drugs except simple aperients (sulphate of magnesia and senna). On that date the pressure was 230 mm. On May 5th it was 234 mm., and on the same day she was ordered iodide of potassium gr. v *t.d.s.* On May 10th the pressure had fallen to 202 mm., on the 17th it was 185 mm., and on the 24th 187 mm. Menstruation occurred from May 13th till May 18th.

* The normal systolic arterial blood-pressure may be taken as between the limits of 100 and 130 mm. of mercury.

Here we see a marked apressor effect of iodide of potassium.

No. 2.—R. E—, male, æt. 51 years. Aortic incompetence with arterio-sclerosis. Admitted to hospital June 7th, 1907.

On admission his pressure was 198 mm. He was ordered a pill of calomel (gr. j) and colocynth *p.r.n.*, to be followed by a saline aperient. On June 14th there was no alteration in the pressure. On that date he was, in addition to the above treatment, ordered iodide of potassium gr. v *t.d.s.* As the result of this the pressure fell by the 21st to 176 mm. On the 28th, however, it had risen to 192 mm.

This case again illustrates the apressor effect of iodide of potassium, the subsequent rise being presumably due to too long continued rest in bed.

No. 3.—C. C—, female, æt. 50 years. Arterio-sclerosis, extreme cardiac hypertrophy. Admitted to hospital October 24th, 1907.

The pressure was then 256 mm. (sitting up). She was given milk diet and simple aperients (sulphate of magnesia, senna, etc.). On October 31st the pressure had risen to 268 mm. That night she was given calomel gr. iv followed by a saline aperient, as the result of which the pressure had fallen the following day (November 1st) to 249 mm. On that date she was ordered iodide of potassium gr. v *t.d.s.*; fish and eggs also were added to the diet. On November 3rd she was ordered a pill of calomel (gr. $\frac{1}{2}$) and pil. rhei co. gr. iv on alternate nights. As a consequence of these measures the pressure on November 7th had fallen to 234 mm. The following day, November 8th, chicken was added to her dietary, and on the 9th the iodide of potassium was omitted. On November 14th the reading was 250 mm. On that day she was ordered sodii nitritis gr. ij *t.d.s.*, but this was omitted on the 20th as she had complained of headache and pain in the back. On the 21st inst. the pressure was 253 mm. From the 23rd onwards she was allowed up for one hour daily. On the 28th the pressure was 251 mm. She was ordered on that day calome gr. $\frac{1}{6}$ two-hourly whilst awake, but this was discontinued on the 29th inst. On that date the pressure was 239 mm. She was the same day ordered erythrol tetranitrate gr. $\frac{1}{2}$ *6tis horis* (this was temporarily omitted from November 30th to December 2nd) and also a pill of calomel gr. j and colocynth *p.r.n.* followed by a simple aperient. On December 5th the pressure had risen to 277 mm.

That day she was ordered iodide of potassium gr. vij *t.d.s.*, also calomel gr. $\frac{1}{6}$ two-hourly during the day, and on the 6st inst., when the reading was 265 mm., the erythrol tetranitrate was omitted. From this time the patient did badly. On the 12th inst. there were marked signs of mercurial stomatitis and she felt ill. Her pressure on that day had fallen to 209 mm. She was ordered a mouth-wash and the getting up was discontinued. On the 13th inst. the pressure was 207 mm.; on the 14th the calomel was omitted and the iodide reduced to gr. v, and she was ordered milk diet. On the 19th inst. the pressure was 210 mm., and the mouth condition was improving.

This case I think shows clearly the apressor effect of calomel alone or combined with iodide of potassium, together with the inefficacy of mere rest in bed. The ill-effects noted above may perhaps be ascribed partly to an idiosyncrasy as regards the effects of mercury and in part to the fact that the reduction in pressure was pushed too far.

It is further interesting to note that this patient had a sister under my care, who not only, be it noted, exhibited an almost equally high blood-pressure, but also a similar idiosyncrasy as regards the effects of mercury.

No. 4.—H. D—, male, æt. 44 years. Chronic interstitial nephritis, right pleural effusion. Admitted to hospital November 22nd, 1907.

On admission the pressure was 273 mm. The right pleural cavity was tapped, two and a half pints of clear fluid being removed, and as the result of this the pressure fell to 243 mm.

On admission he was ordered milk diet. This was followed a few days after by fish. On November 29th the pressure was again 273 mm. He was on that day ordered calomel gr. $\frac{1}{6}$ two-hourly during the day. On December 6th the pressure was, however, still 273 mm. On that day he was ordered iodide of potassium gr. v *t.d.s.* On December 13th the pressure had fallen to 256 mm. That day he was ordered calomel gr. iij *nocte p.r.n.*, and from that date onwards was allowed up for one hour daily. On December 16th he was ordered mixed diet occasionally. His pressure on December 20th had fallen to 220 mm.

This case illustrates well the effect of the removal of a pleural effusion in lowering the blood-pressure, likewise the apressor effect of iodide of potassium.

No. 5.—H. B—, female, æt. 43 years. Arteriosclerosis, cardiac hypertrophy, mitral stenosis. Admitted to hospital May 14th, 1908.

All the observations in this case were made whilst the patient was propped up in bed, and were taken on the forearm. On May 15th the pressure was 225 mm. Later in the evening a reading of 223 mm. was obtained. Immediately after this a capsule of amyl nitrite was given to inhale, during which time the two following observations were made (the first one immediately after the inhalation was begun): 210 mm. and 232 mm. Directly after the administration the following records were obtained at intervals of about five minutes: 241 mm., 238 mm., 220 mm. On the 18th inst. the patient was ordered potassium nitrate gr. x, sp ætheris nitrosi ʒss., liq. ammoniæ acetatis ʒij *t.d.s.*, and also ordered a diet of fish or chicken. The potassium nitrate mixture was omitted on the 21st inst. On May 22nd the pressure was 230 mm. On that date she was ordered iodide of potassium gr. v *t.d.s.* and calomel gr. $\frac{1}{6}$ *4tis horis*. On May 29th, however, the pressure had risen to 255 mm., and on June 5th to 265 mm. On that date the calomel was omitted. On June 12th the pressure was 260 mm., and on that date the iodide of potassium was omitted and erythrol tetranitrate gr. $\frac{1}{4}$ *t.d.s.* ordered. On June 19th, however, the pressure was still the same. From this time onwards she was put on a mixed diet and allowed to get up for a gradually increasing number of hours, and on June 23rd was ordered calomel gr. iij *nocte p.r.n.*, but the pressure on June 26th was still 259 mm.

The prominent feature in this case was the inefficacy of treatment by drugs or rest in bed in reducing the blood-pressure, in fact immediately after the inhalation of nitrite of amyl the pressure was markedly higher than before.

These cases illustrate well the apressor effects of iodide of potassium and of calomel in cases of high blood-pressure, as well as a similar result due to the removal of a pleural effusion. They also confirm the experience of other observers in regard to the ineffectiveness of the nitrites and organic nitrates in such conditions, and one of them (No. 5) shows that sometimes all drugs are powerless to reduce blood-pressure in these cases. It is likewise apparent that in some instances continued rest in bed does not cause a fall in blood-pressure, but whether or not as the result of deficient elimination, has distinctly the opposite effect.

Note on the Prognosis of Cases of High Arterial Blood-Pressure.

The following record of cases of high arterial pressure under my care, whilst not including a sufficiently large number to allow of any dogmatic conclusion, is certainly striking.

Of seventeen cases showing a blood-pressure of upwards of 200 mm., which first came under my observation in the years 1906 and 1907, I have been able to follow up thirteen, of whom eight have died and five are still living (February, 1909). Two of the cases died from cerebral hæmorrhage, three as the result of chronic interstitial nephritis, one from "heart trouble" (this patient had aortic incompetence), and two from unknown causes. Moreover, the longest interval between the date of first observation and that of the death of any of these eight cases was a year and a quarter.

June 28th, 1909.

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A LECTURE

ON

ECTOPIC PREGNANCY FROM THE PRACTITIONER'S STANDPOINT.

Delivered at the Polyclinic.

By G. HERMAN, M.B., F.R.C.S.,
Consulting Obstetric Physician to the London Hospital.

LADIES AND GENTLEMEN,—The title of this lecture has been announced as "Some Points in connection with Ectopic Pregnancy." It might have been better stated as "Ectopic Pregnancy looked at from the point of view of the General Practitioner"; that is, from the point of view of the man who is not an expert operator, who does not, and cannot, get much practice in operating, but nevertheless may be called upon at any time, without assistance, to deal with a case of ectopic pregnancy.

Ectopic pregnancy is a dangerous thing in various ways. But I do not think that so large a percentage of cases die as some people estimate; and the mortality now is much less than it used to be, because so many cases are now dealt with at an early stage that in former years would have been allowed to give trouble in the later months.

In nearly all the text-books on gynæcology—certainly in all the old ones—certain symptoms are given by which the diagnosis of early tubal pregnancy is to be made. Those symptoms are due to hæmorrhage; and before hæmorrhage has taken place I believe it to be impossible to make a diagnosis of tubal pregnancy. I have known cases in which specialists have seen cases, examined them, and failed to find any tubal pregnancy, but in which, nevertheless, the patient has afterwards suffered from an intra-peritoneal hæmorrhage. But those cases do not find their way into print. A case recently impressed this on me. I was asked to see a lady who was pregnant for the second

time, and the object of my seeing her was to give an opinion as to whether there was or was not tubal pregnancy. I was given the history of the first pregnancy, which was this: The lady went for her honeymoon to Switzerland, and she had some symptoms which she mentioned to a medical man, a casual acquaintance who was taking a holiday in Switzerland, and he advised her to go home, so that she might consult a specialist. This she did. She came to London, and by this gentleman's advice she went to one whose loss we all deplore, and whom every specialist knows to have been exceptionally thorough and skilful in the examination of such cases, the late Dr. Cullingworth. He examined with his usual care and thoroughness, and the conclusion he came to was that there was nothing the matter. He thought she had over-tired herself. She then went to a physician, who had not such a large surgical experience as Dr. Cullingworth, but a larger obstetrical experience, and he examined her. He could find nothing the matter with her, and agreed with Dr. Cullingworth. A few days later he was sent for, and found this lady suffering from internal hæmorrhage. A surgeon was called, the abdomen was opened, and a ruptured tubal gestation was removed. Suppose that a case of this kind had occurred in a country village; that the lady had been an important person in the village; that she had consulted the local village doctor, who had examined her and said there was nothing the matter; and that she soon after died from internal hæmorrhage, there being no surgeon available at once. There would be a coroner's inquest, at which the pregnancy would be revealed and things not very complimentary would be said about the doctor who had failed to warn the patient of the danger she was in. A case like that is only exceptional in the greatness of the hæmorrhage. A medical man who examines an early tubal pregnancy before hæmorrhage has taken place and fails to detect it is not in the least to blame, because it is impossible that he could detect it. If you go to any museum where there is a specimen of ruptured tubal pregnancy, and look at it, you will see a little sac about as big as a cherry, and you will see the amnion is not tense. Remember that it is movable in the pelvis. How can any man detect such a small and soft thing as that when he feels it through the thickness of the vaginal and abdominal wall, with bowels and their contents in the way. I think it is impossible, and I think that the fact should be generally recognised.

Supposing that the village doctor whom we postulate has examined the patient and has not found anything the matter with her; soon afterwards he is suddenly called, and finds she has symptoms of internal hæmorrhage. What is he to do? Our knowledge of ectopic pregnancy before the time of Lord Lister was almost entirely derived from the examination of cases post-mortem: either cases of pelvic hæmatocele which had suppurated, and in that way caused the death of the patient; a few rare cases of death from internal hæmorrhage; and cases in which the fœtus had been long retained in the abdomen after its death. From these circumstances it resulted that in nearly every case of ectopic pregnancy examined after death adhesions were found, and therefore in some of the old text-books among the causes of ectopic pregnancy there figure prominently adhesions, which were supposed to kink the tube, and in that way obstruct the passage of the ovum and so lead to its arrest in the tube. That is important from the point of view of the general practitioner, because if an operation for internal hæmorrhage involves breaking down of adhesions and identifying the different parts, the operation might be expected to be a difficult one. The reason I speak of this is, that adhesions are not present in the beginning; it is exceptional for ectopic pregnancy to occur in an adherent tube; and when a practitioner finds a patient in danger from internal hæmorrhage he should remember that in all probability the operation is one of the simplest and easiest that he can undertake. If he opens the abdomen he has first to let out the blood and then feel for the diseased tube, which will almost certainly be free from adhesions, pick it up and tie it.

This is the first great risk in the history of tubal pregnancy, and it can be dealt with by the village practitioner if he has learnt to use antiseptics so that his hands and instruments are clean.

The next stage in the progress of these cases is when a tubal mole has formed—that is, a slight hæmorrhage has taken place around the chorionic villi, the blood has clotted, and formed a firm swelling. That condition can be diagnosed, and when diagnosed it should be removed. And that diagnosis

is tolerably easy. The person who examines can feel a swelling by the side of the uterus, and can make sure there is an abnormal swelling, although it may not be so easy to determine the nature of the swelling. But any swelling which is by the side of the uterus is almost certain to be abnormal, and whether it is an ovarian cyst, or a tubal mole, or a hydrosalpinx, it is better for it to be removed, and its removal is within the capacity of an operator of small experience.

In reading accounts, even recent accounts, of ectopic pregnancy and of operations for it, and proposals for operations in ectopic pregnancy, there is one word that still constantly recurs, and that is "sac." People talk about the "sac" of an ectopic pregnancy, and the necessity of removing it. That word "sac" is a relic of the time before Lord Lister, when these cases were only found out after death, and then the fœtus was found lying in a cavity having a lining membrane. This "sac" was either formed by adhesions among the bowels or it was under the pelvic peritoneum. Because there is a "sac" long after the child's death, it does not follow that it was there when the child was living.

When the ovum is fertilised the chorionic villi sink into the mucous membrane of the Fallopian tubes, and the ovum becomes buried in the muscular wall of the tube; it is not in the lumen of the tube at all. The amnion develops as in a uterine pregnancy. When rupture takes place the amount of blood may be so great as to fill the abdomen with blood and cause death. But it may be small in quantity, and may clot and lie about the tube, and so form a pelvic hæmatocele. And a small hæmorrhage may yet be enough to destroy sufficient chorionic villi to kill the fœtus, and if so, fœtus and blood are quickly absorbed. If it has not killed the fœtus repeated hæmorrhages may occur, and so the mass in the pelvis become larger and larger. When that is the case you have a swelling in the pelvis which increases in size. In such a case operation by abdominal section is indicated. If the hæmatocele has killed the embryo and is about to be absorbed, it is generally absorbed quickly. When blood has been poured out lymph is thrown out, and the parts around become matted together by adhesions; the hæmatocele becomes contained in a cavity, the uterus is pushed forward, and its pressure may cause retention of urine. If you find the uterus greatly displaced and the parts very tense you may be assured that the effused fluid is under pressure; it then may be dealt with by vaginal section, and it is not necessary to open the abdomen.

It is possible that the hæmorrhage may take place through the wall of the tube, which may be perforated. It is common to speak of "rupture" of a pregnant tube. The word "rupture" implies the giving way of something under pressure. But the perforation of a pregnant tube is not a case of giving way under pressure, it is a perforation owing to the invasion of the wall of the tube by trophoblasts. This may take place, hæmorrhage may occur, and yet the child may go on growing; and if the perforation is on the part of the tube which is turned towards the peritoneal cavity the fœtus will develop in the peritoneal cavity. The child lies free among the bowels, enclosed in its amnion; while it is living there are no adhesions, and there is no sac. And in operating for a condition like that there is no necessity to think of removing the sac at all; the amnion will come away with the child. It has long been taught that one of the signs of ectopic pregnancy was that when the fœtus was not in the uterus its outline and movements could be felt unusually distinctly. This applies only to cases in which the child is free in the peritoneal cavity.

I have now mentioned four conditions: first of all great intra-peritoneal hæmorrhage occurring early in the pregnancy, producing grave symptoms and threatening to kill the patient, a condition in which the operation is urgently required and is simple and easy. Then with pelvic hæmatocele you have four different conditions: first a hæmatocele which is not large and becomes quickly absorbed, in which case no operation is required. Then hæmatocele, which repeatedly increases in size. In this condition an abdominal operation is called for, but is not a difficult one. Third, a tubal mole, in which also operation is called for, but is a simple one. And then you have blood effused under pressure, which should be let out by the vagina; the operation is simple, and if done with clean hands ought to be successful. These are all operations which any person of average skill ought to do with success.

Supposing the patient escapes both death from hæmorrhage and also arrest of the pregnancy by

the knife of the surgeon during the early months, and the ectopic pregnancy approaches full term, the condition of things becomes altered. When the pregnancy is so far advanced that the child is big enough to have a separate existence, and is in the peritoneal cavity, the operation for its removal is one of the most difficult and dangerous in surgery. The danger consists in the hæmorrhage which results from detachment or cutting through of the placenta. The placenta must be dealt with in some way. At one time it was laid down as a rule that the placenta should not be meddled with, because it was found that the danger of hæmorrhage from its removal was greater than the risk of infection during the discharge of the placenta afterwards. But at present, although the risk attending removal of the placenta is still very great, the results of these later operations show that a larger proportion of patients get well among those from whom placenta is removed than amongst those in whom the placenta is left. So I think it is good practice if an operation is done while the child is living and viable to endeavour to remove the placenta. But it must ever be remembered that the longer the pregnancy goes on the larger the child and the more extensive the placenta, the more difficult and dangerous will be the operation, and even the best results still represent a very high mortality. I know of no collection of the records of operations on extra-uterine pregnancies which includes only cases in which the child was living and had reached the ninth month; cases in which the child's life was allowed to be a leading consideration in deciding as to treatment. The collections of operations known to me include also operations done earlier than the ninth month, with the object, not so much of saving the child's life as of saving the mother the risks contingent upon the continuance of the pregnancy. Supposing the operation is not done, the child may be developing under the peritoneum; rupture happens sometimes in the later months of pregnancy, but it is not so common as in the first three months. When the child is developing in the peritoneal cavity it is difficult to see what there is to rupture. When pregnancy reaches term and spurious labour takes place, the danger of rupture then is very slight indeed. If the case is let alone, then some time afterwards—how long unfortunately we do not know, if we did we could be more positive about the right treatment—the placenta becomes thrombosed and the circulation through it stops, the placenta becomes converted into a solid mass, and the operation is again one of the simplest and easiest conceivable. The only sac is composed of a few adhesions between the bowels, which the surgeon need not trouble about. He can extract the child and peel off the placenta without hæmorrhage, and the result, if he has clean hands and instruments, ought to be quite satisfactory. There is an enormous difference between the operation when the child is alive and an operation after the placental circulation has ceased. One is very dangerous, and the other is very simple and safe. Still, one must admit, when you are called to a patient with a six or seven months' ectopic pregnancy, that although the danger of the operation done when the child is alive is greater than when it is dead, there are dangers which attend the prospect of waiting for the child to die and for the placental circulation to cease. The question is whether the dangers incurred by waiting are less than those of the operation done when the child is alive. I know of no account complete enough to show the actual results of operations performed during the life of the child. To make such a comparison clinically instructive we should have full information about the period of the pregnancy at which the operation was done, because operation at the ninth month is more dangerous than operation at the eighth month, and one at the seventh month is more dangerous than an operation at the sixth month. The great danger comes from the frightful hæmorrhage which attends the cutting through or peeling off of the placenta. After natural delivery patients sometimes die from post-partum hæmorrhage. But there you have a uterus which can be made to compress the bleeding vessels, whereas in ectopic pregnancy there is nothing to compress bleeding points. I think that if a patient with an ectopic pregnancy of six months or more is in circumstances where she can, if internal hæmorrhage occurs, be taken to a hospital at once and there treated, it is better for her to run the risk of such hæmorrhage and to wait until the child has died and the placenta has become thrombosed. I do not say that applies if the patient is in such a position that the surgeon cannot be promptly called to her in case of such a dangerous incident. In such

circumstances it may be better for her to have the operation done without waiting for the death of the child and the thrombosis of the placenta. But if operation is decided on while the child is alive, the sooner it is done the better. The immense risk of the operation when the child has come to term is not adequately compensated for by the prospect of a living child, because the children of these pregnancies are often malformed. Although the operation is still a very dangerous one, yet surgeons are learning now to systematise their procedure. There are methods of dealing with hæmorrhage in these cases which are better than those which used to be employed. In the earlier cases the only plan which seems to have occurred to the surgeon was to peel off the placenta and try to stop hæmorrhage by styptic applications or plugging with gauze. To treat the hæmorrhage caused by separation of a full term placenta by such methods is puerile, and a surgeon who cannot control hæmorrhage in any better way should let the patient incur the risk of waiting for the death of the child. There are two ways in which the placenta of a full term gestation has been satisfactorily dealt with. I have mentioned that the more recent statistics do show that those from whom the placenta has been removed have done better than those in whom it has been left. One method is removing the parts to which the placenta is attached. Remember the pregnancy was originally in the Fallopian tube, and as the chorionic villi spread they will naturally be implanted on the broad ligament, and they may spread on to the uterus. If the pregnancy is not far advanced the placenta will be correspondingly small, and it may be limited to the broad ligament or to the broad ligament and the uterus, and if the surgeon will tie the base of the broad ligament, and is prepared, if necessary, to remove the uterus with the placenta, he can remove the whole placenta and the patient will have a good chance of getting well. But when the case is advanced and the placenta has spread over other viscera in the abdomen—broad ligament, uterus, bladder, abdominal wall, intestine—the only method by which satisfactory results have been attained and can be attained is by many prophylactic ligatures. The operator must enter on the operation prepared to tie any number of vessels. He must be prepared to tie the mesenteric, the ovarian and uterine arteries, and the epigastric artery if necessary, peeling off the placenta after prophylactic ligature of the vessels supplying every part to which it is attached. That is the only way, I think, that these operations in advanced ectopic pregnancy will be made safe.

I have spoken so far of ectopic pregnancy in which the child is developing in the peritoneal cavity. There are cases, which Dezeimeris described long ago as sub-peritoneo-pelvic pregnancies. These have since then been very well described by Dr. Berry Hart, and more recently by Mr. Taylor, of Birmingham. In these cases the fœtus and placenta are underneath the pelvic peritoneum, so that when the abdomen is opened the fœtus is not seen, but instead you find a big tumour rising up out of the pelvis everywhere covered by peritoneum. In these cases there is no sac which must be removed. The child is lying in a cavity in the cellular tissue under the peritoneum, and the only things to be removed are the child and the placenta. And in these cases there is this difference, that if you open the sac from above and extract the child, it may be possible to sew up the peritoneum and then drain the cavity which contained the fœtus through the vagina. If that can be done there is no need to trouble about peeling off the placenta, because it is contained in a comparatively small space, which can be kept clean by frequent irrigation with antiseptic fluid, and the placenta may be safely left to come away. Mr. Taylor has shown that in this situation the child may develop in front of the uterus, lifting up the peritoneum, the uterus being then behind the gestation sac. It may be behind or at the side of the uterus, which will then be pushed forwards or to one side. It is possible that through the vagina you may be able to feel the sutures of the fœtal head, or the outline of the breech. If so it will be better to cut through the vagina and extract the child with the aid of the cephalotribe. For if you can plainly feel the child the placenta is not in the way. There is, then, no need to trouble about removing the placenta, because it may be safely left to come away. If the placenta is attached over a large surface of abdominal viscera you cannot be sure of washing out every recess of the peritoneal cavity—that is impossible. One of my colleagues at the London Hospital tried experimentally in the post-mortem department if he could wash clean the purposely soiled abdominal viscera in a dead body.

He tried it with a hose fixed on to a hydrant, and even then he could not get the abdominal viscera clean by flushing out. But if the fœtus is developing under the peritoneum there is a small cavity, and the child is pressed down into a small space, and the cavity can be easily irrigated and kept clean.

When you have an ectopic pregnancy in the peritoneal cavity with a living child, I still think the best practice to be followed is to wait until the child is dead and the placental circulation has stopped. The dangers after death of the child are those attending suppuration. But it is not difficult to perceive the onset of the suppuration. As soon as suppuration begins the patient will commence to get feverish. The mere fact of suppuration means that the placental circulation has stopped. As soon as suppuration begins the operation should be done. The child being dead and the placenta thrombosed, it is a simple and safe operation.

May I recapitulate the opinions I have put before you in this lecture?

(1) The diagnosis of tubal pregnancy before hæmorrhage has occurred is impossible.

(2) The diagnosis of a tubal mole from some other conditions is difficult, but nearly all the conditions which may be reasonably mistaken for a tubal mole equally require prompt operation.

(3) Slight hæmorrhage from perforation of a pregnant tube is often accompanied by death of the fœtus and rapid absorption of the effused blood.

(4) When great intra-peritoneal hæmorrhage has taken place from perforation of a pregnant tube operation is urgent and simple. The danger from delay in operating is greater than that from inexperience of the operator, if only he be one who understands antisepsis.

(5) After perforation of a pregnant tube the amnion may protrude into the peritoneal cavity, and the child grow free among the bowels, covered only by its amnion. In that case the placenta, as it grows, may become implanted on almost any abdominal viscus, and cover a large area. In such cases it is probable that after the primary preparation the mother runs hardly any risk until after the death of the child.

(6) In such cases operation while the child is viable is an extremely dangerous one, and is more dangerous the more advanced the pregnancy.

(7) The danger is from hæmorrhage resulting from separation of the placenta. The experience of more recent operators shows that it is nevertheless safer to remove the placenta than to leave it to come away. The methods of preventing such hæmorrhage which have proved successful are: (*a*) the removal when possible of the viscera to which the placenta is attached; and (*b*) extensive prophylactic ligature of the arteries supplying the placental site.

(8) If operation is postponed until after the death of the child, some time afterwards (unfortunately we know not exactly how long) the circulation through the placenta ceases, and it becomes thrombosed. If an operation is now done the placenta can be peeled off without hæmorrhage, and the operation is simple and safe.

(9) When the pregnancy is underneath the peritoneum there is danger of rupture at any period of the pregnancy. Therefore in this case the sooner operation is done the better. The peritoneum over the child should be divided, and the child extracted. Then the situation of the placenta should be ascertained. If it is not implanted on Douglas's pouch an opening should be made in the lowest part of this pouch, so that it can be irrigated from the vagina, and then the incision in the peritoneum closed. If the placenta covers Douglas's pouch, then the peritoneum of the placenta-containing cavity should be stitched to the abdominal wall. In either case the pressure within the abdomen will so contract this cavity that it can be kept clean by antiseptic douches while the placenta is coming away.

(10) In no form of ectopic pregnancy is there a "sac" (other than the amnion) which requires removal.

July 5th, 1909.

The Effect of the Injection of Salt Solution into the Intestines on the Gastric Secretion.—V. Benczur, discussing a series of experiments on a dog, cites the work of Cohnheim and Dreyfuss, who showed that if solutions of $MgSO_4$ or NaCl were injected into an intestinal fistula in a dog, that a test meal placed in the stomach remained there longer than when no intestinal injection was made, and also that the $MgSO_4$ caused an increase of gastric acidity, while the NaCl caused a reduction thereof.—*Medical Record*, vol. lxxv, No. 25.

SPINAL ANALGESIA.*

By E. CANNY RYALL, F.R.C.S.I.

MR. PRESIDENT AND GENTLEMEN,—My first duty is to thank you for the honour you have conferred upon me by asking me to open a discussion here this evening on spinal analgesia.

Owing to the limited time at my disposal I fear my remarks must be patchy in the extreme; still, I hope the most recent work I have been doing will interest you, and be the means of popularising a method which to my mind is of the utmost value to suffering humanity.

It may surprise my audience to hear that I now operate on all parts of the body, including the head, neck, arms, and thorax, under the influence of this method. The nature of the operation and the age of the individual make no difference.

You may be a little sceptical when I tell you that I have injected patients between the first and second dorsal vertebræ who have had such operations as craniectomies, excision of the sympathetic, extirpation of the larynx, and excision of one half of the tongue together with removal of the glands from both sides of the neck, performed painlessly and without danger under the influence of spinal analgesia, but such is the case.

I have even injected a little girl, æt. 2½ years, who submitted to an operation on the scalp without the slightest alteration in her general condition.

My preliminary remarks will bear on the subject of respiratory paralysis. As you all know, this is the great danger to be feared when a subdural analgesic injection is given.

If we can prevent this calamity occurring—and we can now do so as you will learn later—the great bugbear to spinal analgesia has vanished.

I will now explain, quoting Heineke and Laewen, how this condition is produced, so that you may more easily understand how we may prevent its occurrence.

Two possibilities at once strike us when we come to consider the causation of respiratory paralysis:

(1) Are they the result of the reabsorption of the drug into the general circulation? Or—

(2) Are they caused by the ascension of the analgesic solution in the dural sac and its direct contact with the vital centres in the central nervous system?

We know that the rapidity of the reabsorption of drugs dissolved in the cerebro-spinal fluid of dogs, on account of the reabsorption surfaces, is generally much more rapid than that of the subcutaneous cellular tissue. The same amount of poison has a much more toxic action in subdural than it has in subcutaneous injections.

That the extension of the drug in the dural sac is the essential cause and that reabsorption into the circulation is quite, or for the greater part irrelevant, is proved by the following experiments:

(1) When novocain in the same dose (0·03 gramme per kilogramme body-weight) and same concentration is injected into rabbits, we find:

(*a*) In intra-dural injections there is always at once intense and persistent fall of the blood-pressure, and frequently death within a few minutes.

(*b*) In intra-venous injections there is an immediate fall of the blood-pressure, but it is of very short duration, and death only supervenes if the injection has been made with great rapidity.

(*c*) In intra-muscular injections there is no action on the blood-pressure which can be recognised.

From this comparison one must draw the conclusion that in subdural injection the reabsorption of the poison cannot possibly be the only cause, and never the chief cause of the poisoning. For no matter how rapidly it may be sucked up out of the dural sac and reabsorbed from the subcutaneous cellular tissue and muscular system, the intensity of the action must still remain far behind as compared with the immediate flushing of the circulation with the poison such as takes place in intra-venous injection, and yet we see much more severe and prolonged poisoning, which moreover runs an entirely different course, in intra-dural injection. This fact can only be explained thus: that the course of the poisoning in intra-dural injection is characteristically not caused through the rapidity of the reabsorption, but through the direct action of the poison on the substance of the central nervous system. It is only after contact with the central organs that the course of the poisoning becomes impressed with the characteristic stamp.

(2) In a second series of experiments, the dural

* Delivered before the West London Medico-Chirurgical Society.

sac was closed before the injection was given by means of a ligature encircling the membranes and cord at the height of the upper thoracic portion of the spine.

When 0·03 gramme of novocain per kilogramme body-weight was injected subdurally below the ligature (which under normal circumstances would without exception cause a violent fall of the blood-pressure, and which frequently resulted in the death of the animal) the blood-pressure did not alter at all.

Injection of the same dose above the ligature generally killed the animal at once.

This second series of experiments proves that the dose of an analgesic which, injected subdurally, always results in severe poisoning and often in death, has no toxic symptoms if we cut off the poisonous path to the medulla and the brain and prevent any direct contact with these organs.

We must draw a conclusion from these experiments, namely, that the contact of the toxic solution with the central organs mnst he regarded as the essential, if not the only cause, of poisoning in subdural injections.

In my opinion the result has but one meaning. With the subdural application of an analgesic solution, poisoning only appears if the drug, by ascending in the dural sac in a toxic quantity, comes into direct contact with the centres of the medulla and brain.

In the dose of novocain employed for spinal analgesia reabsorption cannot play any important part, for the reabsorption from the dural sac by the blood-stream, no matter how rapid it may be, does not produce any intra-dural poisoning with the dose in question.

The dangers of spinal analgesia lie isolated and alone in the direct contact of the injected solution with the important vital centres.

So much for the causation. I will now relate to you how we can prevent the occurence of respiratory paralysis.

To my friend, Professor Thomas Jonnesco, Professor of Surgery in the University of Bucharest, Roumania, is due the honour of making this grand discovery.

At the Jonnesco Institute he investigated a series of experiments on dogs. Briefly they were as follows :

In his first series he worked with pure stovaine. In his second series, to the stovaine he added a stimulant for the nervous system in order to counteract the paralysing action of the stovaine. He had recourse to neutral sulphate of atropine. Later he undertook a third series of experiments, in which he associated the stovaine with neutral sulphate of strychnine. This solution gave excellent results with a large number of dogs, and proved to him that he had found the necessary combination in order to remove the paralysing effect of stovaine on the respiration while leaving its analgesic action intact.

Jonnesco realised that the drugs used for the production of spinal analgesia were all protoplasmic poisons and depressants to the vital centres in the central nervous system.

By utilising a drug with a stimulating action he was able to neutralise the depressing effect produced by stovaine, so that to-day we are in a position to inject the analgesic solution into any part of the spinal canal without fearing respiratory paralysis supervening, and thus able to operate on all parts of the body from the head to the feet under the influence of this method.

Hearing of this discovery I paid a visit to Roumania, where I worked for nearly a month with Jonnesco.

On my arrival I found that he had completely given up using general anæsthetics. All his operations were performed under the influence of spinal analgesia with the greatest success.

As Jonnesco had only worked with strychnine in combination with stovaine, I was most anxious to find out how strychnine would act when incorporated with other drugs. With this object in view I carried out a series of experiments on dogs, using novocain, yohimbin, quinine, magnesium sulphate, etc.

The largest dose of novocain which I injected was twenty centigrammes. This was given in the sub-occipital region. Although the animal got respiratory paralysis, it soon recovered under the influence of artificial respiration.

If you inject even two centigrammes of stovaine without strychnine into dogs respiratory paralysis occurs.

With stovaine and strychnine in combination you can administer up to six centigrammes without affecting the vital centres, but any dose above that causes respiratory paralysis. The maximum dose

of stovaine when incorporated with stychnine which can be given is ten centigrammes. With this dose respiratory paralysis always sets in within a minute or two, and in most cases the dog dies.

These experiments alone will be sufficient to demonstrate to you that in one case you can inject twenty centigrammes of novocain without killing the animal, whereas, on the other hand, you can only administer ten centigrammes of stovaine with a chance of the dog surviving.

Therefore novocain and strychnine form an excellent combination.

I have always maintained that if a drug is injected into the spinal canal all evidence must show this drug to be non-irritating.

Both from the clinical and experimental side we find that stovaine is irritating, and of all the preparations used for the production of spinal analgesia it has the most marked action on the vital centres. On these grounds alone I could never recommend its use. It is therefore a good thing for the patient that strychnine prevents the depressing effect of novocain on the respiratory centre.

I have used this drug now for some years for producing spinal analgesia, and I have never seen any permanent ill-result to follow its use. My experience with novocain and strychnine leads me to believe that it is the best combination at the present day we can employ for producing spinal analgesia in any part of the body.

Tropacocaine is another good drug, but it is more toxic than novocain and the duration of the analgesia produced by it is shorter.

Although I have had the honour of introducing into Vienna and Budapest the method of operating on the head and neck under the influence of spinal analgesia, it was Jonnesco's discovery which enabled me to do so.

One case which impressed my audience in Vienna was most instructive. The patient was a woman suffering from an enlarged thyroid pressing on the trachea and causing marked dyspnœa.

At 7.52 a.m., the patient having been placed in the sitting position, I inserted my needle between the first and second dorsal vertebræ, and injected six centigrammes of novocain and half a milligramme of strychnine, dissolved in 1 c.c. of water. After the injection was given she was kept seated for two minutes, and then placed in the horizontal position with the head low.

At 7.58, *i. e.* six minutes after receiving the injection, Professor Eiselsberg, one of the leading surgeons in Vienna, commenced the operation.

At 8.24 the greater part of the thyroid was excised. It weighed 12¼ ounces.

At 8.34 the operation was finished, the analgesia being perfect throughout. I have had a similar result to this in three other thyroidectomies.

I hope you will understand that children bear spinal analgesia very well. I have on many occasions used lumbar puncture on little patients, more especially when I have found them suffering from intussusception.

For operations on the upper half of the body my experience so far is limited to four cases. They bore the operations splendidly, giving me no cause for anxiety.

I will now pass on to the technique which I employ when giving cervical, dorsal, and lumbar injections.

Cervical Puncture.

Position of patient.—He may be either—

(1) Seated on the operating table with the head bent strongly forward, so that the chin is brought in contact with the thorax, or—

(2) Lying on his right side with the head inclined as much as possible towards the chest and held in this attitude by an assistant.

As a general rule I prefer to make a cervical puncture while the patient is recumbent, and if a second injection has to be given during the course of the operation this is again administered in the same position.

Surface anatomy.—In the middle line of the back of the neck there is a distinct intermuscular furrow—the nuchal furrow. This commences above at the external occipital protuberance, and if the finger be carried down along it from that point the external occipital crest is first felt, and then the prominent spinous process of the axis is encountered, separated from the occipital bone by an interval, which corresponds to the position of the atlas.

As the spine of the axis is one of our landmarks in cervical puncture, and that of the seventh cervical or vertebra prominens is another, it is well to know that the former may easily be felt beneath

the occiput and the latter at the root of the neck, with frequently the spine of the sixth above it.

The spines of the vertebræ between the second and sixth cannot be felt as individual structures, but a ridge indicating their position and that of the ligamentum nuchæ can be distinctly made out.

Site for injection.—(1) *Sub-occipital*: The needle is inserted in the median line midway between the external occipital protuberance and the spine of the axis. It is pushed in perpendicularly to a depth of one and a half to two and a half inches, according to the age and muscular development of the patient.

Owing to the large size of the subarachnoid space in this region a wide interval separates the dura mater from the spinal cord. No anxiety need therefore be feared that the point of the needle will cause damage to the nervous substance.

(2) *Medio-cervical.*—The needle is inserted in the median line midway between the spines of the axis and the seventh cervical vertebræ.

It is pushed in perpendicularly and enters the subarachnoid space between the fourth and fifth cervical vertebræ.

The depth its point has to travel before the cerebro-spinal fluid escapes is slightly less than in suboccipital puncture.

Advantages—Disadvantages.

I have not yet arrived at any definite conclusion as to whether any advantage is to be derived from cervical injections. Perhaps the duration of the analgesia may be prolonged if the injection is made in the neck, but riper experience is required to prove this point.

On the other hand, from the remarks I have already made concerning respiratory paralysis, you can readily understand that if one gives a cervical injection, the cerebro-spinal fluid in the neighbourhood of the bulb becomes so concentrated with the drug that the chances of respiratory paralysis occurring are much greater than if the injection is given in the dorsal region.

Although I have on several occasions injected novocain and strychnine through sub-occipital and medio-cervical punctures without any ill-results following, yet I feel that as all operations on the upper part of the body, *i. e.* head, neck, arms, and thorax, can be carried out with the greatest success through an injection made in the upper dorsal region, I can at the present time see no reason why we should resort to cervical injections.

It is quite another matter when we speak of cervical puncture as a diagnostic method. By this means information of the greatest value may be obtained.

It may interest you to know that if a patient suffering from some brain lesion has a puncture made in the lumbar region and some cerebro-spinal fluid withdrawn, and then a sub-occipital puncture made immediately afterwards and some more cerebro-spinal fluid obtained, the composition of the fluid withdrawn from the two regions will vary to a marked degree. Or two needles may be introduced simultaneously in the same patient, one through the sub-occipital and the other through the lumbar region; the cerebro-spinal fluid which flows from the upper and lower segments of the spinal canal will show a marked difference when submitted to microscopical examination, etc.

Dorsal Puncture.

Position of patient.—He is seated on the operating table with the head bent strongly forward and the chin resting against the chest.

If the patient is too ill to sit up, the puncture may also be made with the patient in the lateral position, with the head inclined strongly towards the thorax.

As a general rule I prefer to insert the needle while the patient is seated, but in cases in which the puncture has to be repeated during the course of the operation this can be done in the recumbent posture.

Surface anatomy.—As the nuchal furrow is traced towards the root of the neck, a prominence is encountered which is formed by the spinous processes of the sixth and seventh cervical vertebræ and of the first dorsal vertebræ. Of these three vertebræ the spine of the first dorsal is as a rule the most prominent, and marks the interval between the nuchal and spinal furrows. They necessarily project more plainly when the neck is inclined forwards. In the spinal furrow proper the spines of the dorsal vertebræ can be made out, and it will be noticed that some slight deviation in their position from the middle line is normal. The spines of the mid-dorsal vertebræ are difficult to feel when the erect position is maintained, but they become more easily palpable when the body is bent forward.

In counting the dorsal vertebræ you may commence above at the prominence formed by the first thoracic spine and enumerate downwards. One can also count from below upwards by defining the twelfth rib which articulates with the lowest dorsal vertebræ. It must, however, be borne in mind that the twelfth rib is often very short and does not project beyond the margin of the erector spinæ, so that the lowest rib that can then be felt is the eleventh. The ribs should therefore always be counted from above downwards and not from below upwards.

In cases of difficulty it is well to remember that the scapula covers the ribs from the second to the seventh inclusive, and its superior and inferior angles and spine can easily be distinguished.

When the arms are hanging by the side the upper angle of the scapula corresponds to the superior border of the second rib, or the interval between the first and second dorsal spines, the lower angle to the upper border of the eighth rib, or the interval between the seventh and eighth dorsal spines; and the inner end of the spine of the scapula to the interval between the third and fourth dorsal spines.

Another method of defining the lower dorsal vertebræ by counting from below upwards is by first demarcating the fourth lumbar spine and then reckoning upwards.

This is the procedure I generally employ.

Site for injection.—The operation about to be performed guides me entirely in this matter. For operations on the—

(*a*) Head, neck, arms, and thorax the first dorsal space is chosen; for the—

(*b*) Liver, gall-bladder, stomach, spleen, pancreas, etc., the eleventh dorsal space is selected; and for the—

(*c*) Kidneys, intestines, herniæ, pelvis, and lower limbs, etc., the choice falls on the twelfth dorsal space.

Insertion of needle.—The needle is inserted in the middle line, between the—

(*a*) First and second dorsal spines for operations on the head, neck, arms, and thorax; between the—

(*b*) Eleventh and twelfth dorsal spines for operations on the liver, etc.; and between the—

(*c*) Twelfth dorsal and first lumbar spines for operations on the kidneys, intestines, pelvis, and lower limbs.

It should enter immediately below the bone, and be pushed forward with a slight upward inclination.

A great point must be made of passing the needle very slowly, and at the same time carefully watching for the escape of cerebro-spinal fluid. Owing to the small space existing between the dura mater and the spinal cord in this region, it is quite an easy matter, if the needle is inserted quickly, for its point to traverse the subarachnoid space and penetrate the substance of the spinal cord without any cerebro-spinal fluid escaping. When the needle has entered the subarachnoid space the greatest care must be taken to keep the patient from moving, in order to avoid its point being withdrawn from the fluid cavity in which it rests, and for a similar reason, during the injection of the anæsthetic, pains must be taken to cause as little movement of the needle as possible.

Dose employed: (1) *Strychnine.*—In discussing the dose of this drug I would like to bring before your notice some particulars concerning the action of strychnine when introduced into the subarachnoid space.

First, you have to remember that the poisonous properties of strychnine are far more active when brought in contact with the spinal cord than when given subcutaneously—in other words, an individual can tolerate a larger dose when the drug is injected beneath the skin, or taken by the mouth, than he can when it is given in the form of a spinal injection.

Secondly, patients can bear much larger doses of strychnine when injected into the lumbar and lower dorsal than they can when the drug is administered into the cervical or upper dorsal regions. For instance, if one milligramme of strychnine is introduced into the subarachnoid space between the first and second dorsal vertebræ, the peculiar change wrought in the nervous system is such that a slight stimulus when operating—or even touching the skin—will cause a tetanic contraction of the skeletal muscles; whereas on the other hand, you can inject one and a half milligrammes of strychnine into the lumbar sac without any such effect being produced.

Thirdly, children cannot tolerate as large an amount as adults. The dose, therefore, varies with the point of puncture and the age of the patient.

For operations on the head, neck, arms, and

thorax, when the puncture is made between the first and second dorsal vertebræ I inject half a milligramme of strychnine, except in the case of children from one to three years of age, to whom I only give a quarter of a milligramme.

For other parts of the body, when the injection is made either between the eleventh and twelfth dorsal or between the twelfth dorsal and first lumbar vertebræ, the dose will be either half or one milligramme, half a milligramme being given to children under ten years of age and one milligramme to patients over that age-limit.

(2) *Novocain.*—For operations on the head, neck, arms, and thorax, the dose will vary from 0·02 grm. up to 0·06 or even 0·08 grm.

For operations on the liver, gall-bladder, stomach, spleen, pancreas, etc., the amount injected will be from 0·05 grm. up to 0·12 or even 0·15 grm.

For operations on the kidneys, intestines, herniæ, pelvis, and lower limbs, the dose injected will vary from 0·06 grm. up to 0·15 or even 0·2 grm.

From the experience which I have gained in spinal analgesia I now make it a rule to diminish the ordinary dose of novocain when I am called on to operate on patients suffering from any of the following conditions:

(*a*) Severe traumatic lesions.

(*b*) Grave hæmorrhage.

(*c*) Collapse from any cause, *e.g.* strangulated hernia.

(*d*) Anæmia.

(*e*) Cancerous cachexia.

In these cases small doses of the drug at once produce the required analgesia and its duration is prolonged, notwithstanding that the quantity of novocain which has been injected is diminished.

Again, when scopolamin and morphia are given as adjuncts to spinal analgesia I follow the same rule of diminishing the dose.

(3) *Water.*—One c.c.

Method of preparing the dose.—The method of preparing the solution which I adopt is as follows: I keep by me three sterilised solutions of the sulphate of strychnine of different strengths. One contains a quarter of a milligramme, another half a milligramme, and a third one milligramme of strychnine in each cubic centimetre of water. These strychnine solutions have to be prepared some hours before they are required, as it takes time to properly dissolve the drug in water.

The doses of novocain are kept in powder or tablet form already sterilised in glass tubes.

One cubic centimetre of the strychnine solution of the required strength is then drawn into the syringe and injected into the glass tube containing the novocain, and the whole thoroughly mixed together by drawing backwards and pushing forwards the solution from the glass tube into the syringe.

I have also had the drugs put up already mixed together and kept in solution in sterilised glass ampullæ.

So far I have found no difference in the action of the drugs when they are kept in ampullæ, or mixed immediately before use.

Injection of the analgesic solution.—A successful puncture is indicated when the cerebro-spinal fluid escapes freely, and unless this occurs the injection must not be given.

In dorsal injections I make it a rule not to withdraw any cerebro-spinal fluid, for I have found that the more liquid one withdraws the more rapid is the diffusion. As our object is to make this as slow as possible, the novocain solution is injected directly the point of the needle has entered the subarachnoid space.

In all spinal injections the analgesic solution must be introduced slowly, especially in the upper dorsal region. The ordinary piston supplied to a syringe gives no guarantee that the injection is carried out slowly. To avoid this I have had a screw arrangement affixed which completely prevents the sudden emptying of the contents of the syringe into the dural sac.

Position of the patient immediately after the injection.—For—

(*a*) Operations on the head and neck: He is kept seated in the erect position for two minutes (by watch or clock), and is then placed in the horizontal position with the head low.

(*b*) Operations on the upper limbs, thorax, breast, etc.: He is kept seated in the erect position for three minutes (by watch or clock), and is then placed in the horizontal position with the head and shoulders slightly elevated.

(*c*) Operations on the upper part of the abdomen, *e.g.* liver, gall-bladder, stomach, spleen, etc.: He is kept seated in the erect position for two minutes and is then placed in the horizontal position, with head and shoulders slightly elevated.

(*d*) Operations on the kidneys, intestines, herniæ, pelvis, and lower extremities: He is kept seated in the erect position for five minutes, and is then placed in the horizontal position with the head and shoulders slightly elevated.

(*e*) If the operation requires the Trendelenberg position the patient is kept seated in the erect position for six minutes. He is then placed in the horizontal position so that the abdomen may be washed, and when this procedure is finished the table may be tilted as required.

Lumbar Puncture.

(1) *Position of patient during injection.*—Before proceeding further I should like to bring before your notice an anatomical point of the greatest importance in connection with lumbar puncture, for upon the knowledge of this depends in a large measure your success with this method.

As the nerve-roots forming the right and left halves of the cauda equina descend in the lumbar sac, they are separated from each other by a narrow elongated space which is full of fluid. In the depth of this fissure, seen from behind, the point of the conus medullaris and the filum terminale lie. This cleft, which is broader above than it is below, is about two to five millimetres wide in adults. It is generally more pronounced in children, in whom the cauda equina is altogether looser. This space was first described by Quincke. Doenitz has recently named it the "cisterna terminalis," not on account of its size, but because of its clinical signification, which is analogous to similar formations in the medulla, cerebellum, and cerebrum.

As the fissure lies between the right and left strands of the cauda equina I think a more suitable name for it would be the "cisterna caudalis," and as such I will describe it in this paper.

Doenitz has drawn attention to the fact that if the cisterna caudalis is attained by the puncture, then the cerebro-spinal fluid will flow in a stream, and if the anæsthetic solution is injected into this narrow, elongated space, it can be freely extended in all directions, especially upwards. The collective nerves are stirred up, and we obtain a regular, complete, and extensive analgesia.

If, on the other hand, the point of the needle has penetrated between the nerves forming one half of the cauda equina, the needle aperture may be entirely or partially blocked by a nerve, and the flow in this tubular system from purely mechanical reasons may be absent or only proceed slowly.

The anæsthetic which is injected here is caught between the nerves of the cauda, and can only be extended with difficulty. Therefore the first duty of our technique must be that we learn how to attain the cisterna caudalis with the needle, and we succeed in doing this by making the puncture as accurately as possible in the median plane.

The maximum flow of fluid proves that we have attained our object.

If the fluid only flows slowly we have no guarantee of having obtained the most favourable position for lumbar puncture.

A further reason why this is just the place in which the anæsthetic must be deposited is that it is only here that the raised pelvic position can develop the action we demand of it, namely that by the change of position the ascending stream of fluid takes the anæsthetic up with it.

If the anæsthetic is injected between the tissues of the cauda it is enclosed between the nerves, and there cannot follow the ascension of the fluid in the raised pelvic position. In fact my observations taught me that the raised pelvic position was useless when I had reason to believe that the hollow needle had penetrated into the nerves of the cauda, but when I could assume that I had penetrated the cisterna caudalis from the rapid flow of fluid, then the success of the raised pelvic position was the rule, and was also remarkable for the significant further ascension of the anæsthesia.

In the first, or sitting position, the patient is seated crosswise on the edge of the operating table, with the head bent forward and with the most pronounced kyphotic curvature of the lumbar and dorsal segments of the spine, so that the back is rounded to its maximum, without lateral bending or torsion, with the arms hanging straight down. An attendant stands in front of the patient, who places his head on the attendant's shoulder.

In the second, or lying position, the patient rests either on his left or right side close to the edge of the table, with his chin as near as possible to his drawn-up knees, so that the vertebral column is arched, with the object of increasing the space between the lumbar spines. The flexure of the column may be increased and fixed by an attendant, who encircles both the head and lower extremities in his arms and tries to bring them near together.

Our object in introducing a needle into the lumbar sac is to hit off the cisterna caudalis, and this can be most readily accomplished when the patient is in the sitting posture. I therefore make it a rule whenever I can to place him in this position for injection.

In acute inflammatory affections of the abdomen, and in other conditions when the sitting attitude gives rise to pain or faintness, the patient may be injected lying down, but the chief drawback to this position is the uncertainty of accurately inserting the needle into the middle line of the dural sac, and thus reaching the caudal cistern.

(2) *Surface anatomy.—Lumbar*: With thin people it is easy to count the lumbar spinous processes, which are more isolated from each other than the dorsal. A good landmark is the fourth lumbar spinous process, which in the adult male lies in a horizontal plane with the highest points of the iliac crests. In females, however, this transverse line, passing from the summits of the iliac crests, defines the interval between the third and fourth lumbar spines.

(3) *Methods of puncture.*—There are two methods of puncture by which we are able to gain entrance to the lumbar sac, viz. the *median* and the *lateral.*

When the *median* method of puncture is employed correctly, the needle is inserted through the median plane into the cisterna caudalis.

On the other hand, when the *lateral* method is used, the needle pierces the skin at one side of the median line, and is directed towards the median plane, with a view of entering the caudal cistern. This object may be attained, but on many occasions the point of the needle rests between the nerve-fibres forming the right or left half of the cauda equina.

The chief point is that the meninges should not be injured more than necessary, but only perforated once, whereas, when the puncture is made at the side of the median line, in many cases they have often to be pierced several times for exploration purposes until the fluid can flow freely. I have employed both methods on many occasions, and have decided altogether in favour of a puncture in the median line.

The accidents which are avoided by this proceeding, and to which attention has been drawn by Doenitz, are as follows:

(*a*) The extremely painful sensation when piercing the bundle of nerve-fibres of the cauda is disposed of; formerly, with the lateral method I often experienced this, and, indeed, regarded it as a pretty sure sign that the needle had entered the dural sac.

(*b*) Unnecessary injury to fibres is avoided, and, contrary to what occurred formerly, I have hardly ever seen any fluid coloured with blood.

(*c*) It is not possible to inject an anæsthetic solution between the fibres of the cauda and obtain a good result. The solution deposited in this place will for the greater part be retained for a considerable time in the spaces between the nerves and cause local irritation.

Similar irritation appears also to be caused by bleeding in the same place. The results of the numerous injuries are shown in hyperæsthesia, anæsthesia, paræsthesia in the sensory spheres, and in paralysis and spasms in the motor regions, according to whether the needle-point was in the posterior sensory or an anterior motor domain at the time of injection.

Under some circumstances these disturbances can be of a very unpleasant and tormenting nature, and it is therefore important for us to avoid accessory damage while puncturing in the manner given and thus prevent the bad after-effects.

Semi-lateral analgesia was formerly frequently observed, and was supposed to be due to the position which the patient had assumed during or directly after the injection.

Further research showed that the cause of the phenomena was not due to the influence of weight or gravity, for a patient may be injected lying on his right side, and the upper or left side may become analgesic. And again, a patient may be punctured in the sitting position, and semi-lateral analgesia may follow when the influence of weight could not be construed.

The simplest way of explaining the whole phenomenon is by experimental injections on the dead body.

If one slowly injects Chinese ink into one half of the cauda equina one can see how this will course indistinctly through the dura, but on the contrary very clearly if it can go through the length of the arachnoid without hindrance, when the colour extends at first almost exclusively upwards and downwards between the fibres. It is only later that the ink spreads in width also. The cause of

this manner of widening is easy to understand. The bundle of nerve-fibres of the cauda lie more or less close together, and enclose between them lengthwise scattered, tube-like, hollow spaces, which one can compare to a bundle of round pencils. The ink is first conducted through the canals; it is only secondly that it is widened out in a crosswise direction through the fissures between the nerves.

Let us suppose that instead of ink an anæsthetic solution is injected, then the appearance of semi-lateral analgesia is easily explained. It also became clear why the phenomenon described only appears if the place of puncture lies at the site of the middle line, for it is much easier to effect an entrance in either the right or left half of the cauda.

The observation has often been made, and I have found it confirmed, that when there is a rapid flow of fluid the analgesia is good; but when, on the other hand, the flow is clogged and coming in slow drops, there is frequently strikingly bad anæsthesia.

Everyone who has made a lumbar puncture knows how the flow of fluid varies. At one time it will spurt out in a stream, at another it comes slowly and hesitatingly, drop by drop, or there is apparently no fluid at all, although the needle is certainly in the arachnoid cavity.

When the flow of fluid from the puncture is slow it does not in any way prove that there is a diminished pressure. This is of great importance, with regard to the question of lumbar anæsthesia, to know that when there is a sluggish flow there is nearly always a mechanical hindrance present, and as a rule it is sufficient to simply twist the hollow needle round, push it backwards and forwards, or to make a fresh puncture nearer the median line, in order to change the slow dropping into a flowing stream or into a spurt. As I have noticed that when the anæsthesia is poor the flow of fluid is often extremely slow, I make a principle of obtaining the maximum rapidity for the fluid before I inject the anæsthetic.

(4) *Site for injection.*—I now seldom employ lumbar puncture, for experience has taught me that the resulting analgesia is much better when the injection is deposited into higher segments of the subarachnoid space.

For small operations on the rectum, for hæmorrhoids or fistula, and for operations on the external genital organs of both sexes I occasionally make use of lumbar puncture, and insert the needle either between the second and third or third and fourth spines.

I employ the following method in order to find the fourth lumbar spine: a sterilised towel is laid on both sides of the lumbar region—it prevents our having to disinfect this part—the crests of the ilium are examined by palpation with both hands, and the spinous process, which lies in a connecting line, is defined by spanning the hands, and is then marked with the thumb. From here one counts upwards or downwards in order to find the space selected for puncture.

The next step is to render the space anæsthetic for the painless insertion of the needle, and for this purpose the spray of ethyl chloride is employed. As the skin now becomes frozen at this spot I use a puncture knife for its penetration. By this means two objects are obtained:

(*a*) It renders the procedure more aseptic, as the needle is not likely to become contaminated with micro-organisms from the skin.

(*b*) It prevents the point of the needle becoming blunt by its passage through hardened tissue.

(5) *Insertion of needle.*—This is of the greatest importance, for upon a successful puncture the resulting analgesia depends.

The needle should be passed immediately below the spinous process which bounds the space, and directed forwards and slightly upwards. If it is inserted immediately above the spinous process it is apt to impinge on bone and give rise to pain at the time, which may persist for two or three days. It should then be drawn back a little and inclined further upwards and pushed onwards.

I make a point of first inserting the needle for about three quarters of an inch, for occasionally it tends to incline sideways, and after again convincing myself that it is exactly in the middle—the best way being by looking down upon it from above and altering it if the direction should be wrong—it is passed slowly forward, exactly in the median plane, and, as a rule, after penetrating the somewhat tense arachnoid the cerebro-spinal fluid flows out in a stream. The quantity of fluid which flows through the needle varies widely, for sometimes it comes in a stream, at others only drop by drop, or no clear fluid may come at all, although one is certain of having attained the dural sac. Under all circumstances the appearance of clear

fluid must be waited for before the anæsthetic is injected, as otherwise we have no certainty that the needle-point has really penetrated the subarachnoid space.

The depth to which the needle must be inserted before the fluid flows varies from 1½ inches to 3½ inches. In the case of big, muscular men the depth can be from 3 to 3½ inches, and with very stout people as much as 4 inches.

In rare cases where there is œdema of the skin this must be taken into account, and at the moment of making the puncture it must be disposed of by pressure as much as possible.

In the case of children the dural sac is reached at a depth of half to one inch from the surface, and with them lumbar puncture is a very simple affair, as the slender lumbar vertebræ have a wide, somewhat rhombic space between them, and here, where the spinous processes and ligaments are still but slightly developed, the needle can be inserted in the centre of two spinous processes exactly in the median plane.

When one is convinced that the point of the needle rests in the dural sac and yet no fluid flows, a stylet should be passed through its canal in case it is blocked by a piece of tissue or blood-clot and the stylet withdrawn. If no fluid now comes the needle should be twisted, pushed forward, or drawn backward in case the orifice is occluded by nerve-fibres. This manœuvre failing to give vent to fluid, an obstruction bandage should be applied to the neck. This causes an engorgement of the veins of the brain and venous sinuses, and hence an increase in intra-cranial pressure, which forces the cerebro-spinal fluid downwards. The obstruction bandage has been my sheet anchor in three cases, where, following a successful entrance into the dural sac, I was unable to obtain fluid. Twisting, as well as moving backwards and forwards the needle was of no avail, nor was a second puncture in another space of any use; it was only when I applied the constricting bandage to the neck and waited for a few minutes that the flow of cerebro-spinal fluid demonstrated that the needle-point was free in the subarachnoid cavity, and I was able to inject the anæsthetic, for my golden rule in spinal analgesia is—"Never inject until fluid flows."

I have but rarely found a flow of blood from the needle since adopting the median method of puncture. At the commencement of the flow the cerebro-spinal fluid may be mixed with a little blood, but it soon becomes clear. If blood continues to flow out of the needle then this is not in the dural sac, and has injured the extra-dural venous plexus. The injection must not be given if the blood is flowing continuously, but another puncture made in a fresh place.

When a suitable position for the flow of cerebro-spinal fluid has been found it is advisable to keep the needle firmly fixed in the dural sac during the injection.

Many cases of failure to obtain analgesia are due to the needle having been withdrawn from the subarachnoid cavity, and the fluid injected into the surrounding tissues instead of into the caudal cistern.

Dose employed for operation on the rectum and external genital organs.—Novocain 0·06 to 0·15 gramme according to the age of the patient; strychnine 0·001 gramme (1 milligramme); water 1 c.c.

Position of patient immediately after injection.—He is kept seated for five minutes and then placed in the horizontal position.

I make a point of asking the patient as few questions as possible respecting the sensibility of the skin in order to avoid causing unnecessary excitement. One must never ask, "Do you feel that I am pricking you?" or, "Do you feel that I am cutting you?"

A few minutes after the injection I estimate the condition of the tendon and skin reflexes on the part for operation, knowing that the reflexes disappear a minute or two before the appearance of analgesia. Therefore, the disappearance of the knee-jerk and cremaster reflex is the early sign that analgesia will be perfect in the leg; and in a like manner the absence of the lower, middle and upper abdominal reflexes indicates commencing analgesia in the abdomen. This simple method does not give the patient any pain or anxiety.

In conclusion I may say that time will not allow me to enter more fully into many points connected with spinal analgesia.

I trust, however, that the brief description which I have given of the technique which I employ at the present day will be sufficient to bring forth a good discussion on spinal analgesia—a method which I think has not received that attention in this country which it merits.

July 5th, 1909.

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THE DIAGNOSIS AND TREATMENT OF TUBERCULOUS GLANDS.*

By ARTHUR LATHAM, M.D., F.R.C.P.,
Physician to St. George's Hospital, etc.

THE principles involved in the diagnosis and treatment of tuberculous glands are exactly the same as those involved in the treatment of any tuberculous infection. What is perhaps of even greater importance, they are the same as those involved in the treatment of any infective disease. Whether we are dealing with tuberculous, pneumococcic, staphylococcic, streptococcic, gonococcic, coli, or other microbic infection, the diagnosis depends upon the proof that the particular micro-organism is present, and that its toxin is being absorbed to a greater degree than the resistant forces of the body can deal with adequately; whilst the treatment depends upon placing the patient under the best possible conditions for increasing the natural capacity of the body to resist disease, and upon the intelligent and scientific attempt by the appropriate application of vaccine therapy and other older methods to raise the patient's immunising capacity against the specific micro-organism and its toxic products.

In the diagnosis of tuberculous glands we have to show that the tubercle bacillus is present, and that its toxic products are having a definite effect upon the glandular tissue. It is possible to diagnose the presence of tuberculous glands upon purely clinical considerations in a large number of instances. If, however, we depend on clinical features alone for our diagnosis, our percentage of error must be considerable, and in some instances the results may be disastrous. Medicine is fortunately becoming more scientific, and it is imperative for us to reduce our percentage of error in

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diagnosis by every means in our power. A number of specific tests of the presence of tubercle bacilli as the causal agent of enlargement of glands have been before us during the last few years. Some of these are still upon their trial, but we may safely base our diagnosis upon the results obtained from injections of Koch's old tuberculin or from a series of determinations of the opsonic index in competent hands, with the assurance that our percentage of error will be very largely diminished as compared with our percentage of error if we confine ourselves to purely clinical considerations. The tuberculin test is too well known to need more than this passing reference. With regard to the value of the opsonic index there is at present a sharp difference of opinion in the profession. A discussion on this point would be out of place at this meeting, but I would put it on record that personally I am convinced, from a close study not only of tuberculosis in its various forms but also of other forms of infective disease during the last two years, that the opsonic index is a reality, that Sir Almroth Wright's work has been, and will continue to be, of immense value in the diagnosis of infective disease, and that it has thrown a flood of light upon the pathological processes of this type of disease which cannot fail in the course of time to enhance materially the results obtained by medical treatment, not only from the point of view of immediate "cure," but also from the point of view of diminishing the tendency to relapse.

If on clinical considerations we come to the conclusion that we are dealing with an enlargement of the glands which is possibly tuberculous in origin, we may obtain confirmation from the opsonic index in two ways, provided, as I have said, the determination is made by a competent observer. In some instances a single determination of the index may be sufficient. If the clinical symptoms are compatible with the diagnosis of tuberculous glands, and a single determination shows that the index is well outside of normal limits, for example, well below normal limits—·5—or, less seldom, well above normal limits—1·5—the after-history of the case will show that the index was correct. It is, however, wisest to make a more elaborate investigation, for single determinations may be misleading, whilst a single determination of the index which shows it to be within normal limits is of no value. The opsonic index has proved that in infective disease auto-inoculation is either taking place naturally, or can be made to take place by means of movement. If a greater quantity of lymph and blood is made to pass through a tuberculous gland in a given time, then, although the percentage of toxic products taken up may be the same, yet the total quantity of these products thrown into the general circulation in a given time is greater. This sudden access of tuberculous products naturally has a definite effect upon the immunising response of the blood, and this effect can be measured in a specific way by means of the opsonic index. If we massage a gland gently for a sufficient time, say half an hour, more lymph and blood passes through the gland in that space of time than when the gland is at rest. If we take the opsonic index before massage, and again when this procedure is finished, and again an hour or two later, we will find that in the case of a normal healthy gland the indices are approximately the same, *e.g.* 1·1, 0·9, 1·0. If the gland is tuberculous, the indices will show considerable fluctuations; it may be that as the result of the larger quantity of toxic products thrown into the circulation by massage the index is raised for a time, or it may be that it is depressed. We may have (1) before massage 0·7, (2) immediately after massage 1·5, (3) two hours after massage 0·8; or we may have in another case, (1) before massage 1·1, (2) immediately after massage ·7, (3) two hours after massage ·4. In both these instances the diagnosis of tuberculosis would be positive. In using the opsonic index to establish a positive diagnosis it is essential either that the index should be well outside the normal limits of 1·2 or ·8, or that under the influence of auto-inoculation there should be a considerable difference in the readings as compared with the reading taken at rest. The opsonic index used intelligently is of great service in diagnosis, but its findings must be interpreted with a certain degree of common sense, and must be correlated with the clinical condition.

The question of an accurate diagnosis is all important. Further, too much stress cannot be laid on the importance of arriving at a diagnosis in an early stage of the disease. The responsibility of the profession in tuberculous affections is great, for the simple reason that an early diagnosis often means the difference between comparatively rapid recovery of health on the one hand, and prolonged suffering, and in some cases life-long misery.

on the other. It is not too much to say that the overwhelming majority of all cases of tuberculous disease, if we exclude such acute affections as meningitis and other examples of miliary tuberculosis, are eminently curable by the methods at our disposal, provided that a correct diagnosis is made in a sufficiently early stage to permit of adequate treatment being undertaken in time.

When we have satisfied ourselves by definite evidence that we are dealing with tuberculous glands, on what lines are we to conduct the treatment? Our main dependence must be upon the scientific use of tuberculin, to which fuller reference will be made later. At the same time we cannot afford to depend wholly on tuberculin. Those who trust to the effect of Nature, and especially to the effect of the air at such places as Ramsgate and Margate, obtain a number of satisfactory results, but in many instances the reward of this form of treatment is prolonged ill-health, coupled with unsightly scars or even disaster. Those who trust wholly, or almost wholly, to the effect of tuberculin, whether its administration is controlled by frequent determinations of the opsonic index or not, also obtain a number, possibly a larger number, of satisfactory results, but here again in many instances the results are often disappointing and sometimes disastrous. The same may be said of those who trust wholly, or almost wholly, to surgical procedure, or to the use of Röntgen rays. It is an established fact that natural methods of repair, the use of tuberculin or of Röntgen rays, or the adoption of surgical measures all do good, but that each one of these when employed by itself alone frequently fails. Far better results will be obtained in future by an intelligent use of these methods side by side in an individual case. The clinician cannot afford to neglect the use of tuberculin or of Röntgen rays, or methods which are similar in their action. Nor can the bacteriologist afford to disregard the ordinary and established lessons of clinical observation. Certainly the bacteriological therapeutist cannot afford to trust entirely to the effects of tuberculin or be guided entirely by his opsonic readings; he cannot afford to neglect Nature, for though we may assist Nature and even guide her, we cannot afford to despise her. The surgeon at the present time is a necessary evil so far as tuberculous glands are concerned, but when this condition is diagnosed in an early stage, and treatment carried out efficiently on modern lines, the surgeons will have less to do in this direction. It is probable that the clinician of the future, who, after treating a case of tuberculosis which has come under his notice in an early stage, has to resort to surgical measures, will feel that such a necessity reflects upon his capacity and efficiency.

Before any case of apparent glandular tuberculosis is treated, a thorough examination of the patient should be made. Tuberculosis of the external glands is frequently associated with other tuberculous manifestations, and if we do not investigate each case thoroughly before commencing treatment the line of treatment adopted may be wrong and the result unsatisfactory. One case of several which have come under my notice will serve to emphasise the importance of this point. A young woman sought the advice of a bacteriologist for a considerable enlargement of the cervical glands. The clinical investigation was confined entirely to the swelling, and no examination was made of the lungs. A diagnosis of tuberculosis was made by the blood test. A course of tuberculin was given for some months. The opsonic curve obtained was said to be satisfactory as it was always above the normal limits. No local improvement followed, and gradually the patient became very ill. When she left the bacteriologist and came under my care at St. George's Hospital she was suffering from extensive disease of both lungs, and had high fever. The case was now a hopeless one and ended fatally. I have little doubt that if the first examination had been thorough, or if even the temperature record had been taken, this woman's life would probably not have been sacrificed. The fact that the opsonic index was nearly always above normal misled the bacteriologist who was trusting to one control, and one only.

Any person suffering from glandular tuberculosis should be placed under the best possible natural conditions. Fresh air, good food, and the avoidance of fatigue are necessary to raise his natural resistance. Measures like these, as is known to all clinical observers, greatly enhance the value of vaccine therapy. It is no doubt possible to raise the opsonic content of the blood by tuberculin, but a consideration of this factor does not give us an adequate idea of the whole immunising capacity of the body, and the other factors of

immunity are materially strengthened by the measures to which allusion has just been made. Secondly, in any case of glandular tuberculosis it is important to avoid all sources of irritation. I have seen several cases in which the omission of this precaution has led to disappointing results from the administration of tuberculin in the hands of highly competent bacteriologists. In two cases of glandular tuberculosis of the neck, tuberculin had been given for as long a period as fourteen months without improvement at the time I was consulted. In both cases there were a number of carious teeth in the lower jaw, the presence of which had been overlooked. When these received proper attention, and the source of irritation was removed, improvement at once followed the further administration of tuberculin. In another case a tight elastic hat-band beneath the chin kept up chronic irritation which prevented improvement; in another the clothes round the neck were so tightly fastened that the glands were constantly irritated; in another the presence of pediculi had been overlooked. All such forms of irritation should be avoided if we are to obtain the best results in a reasonable time. In cases in which the cervical glands are involved the condition of the mouth should be ascertained and strict cleanliness maintained. It is particularly necessary that *undue* movement of the glands should be avoided, as it leads to excessive auto-inoculation and so militates against an efficient response by the immunising capacity of the body.

If extensive caseation of a gland has occurred, or if a discharging sinus is present, surgical measures have to be considered. The teaching of experience is, that when caseation to any marked degree has occurred the value of tuberculin and other means of treatment is largely negatived, and that even prolonged treatment fails to give us a satisfactory result until an outlet is provided for the necrosed products. Any surgical measures should, however, be combined with the administration of tuberculin. When a discharging sinus is present it is necessary to find out whether secondary infection has occurred, and if so to administer the appropriate vaccine.

We may now turn to the subject of the administration of tuberculin. Evidence is daily accumulating to show that tuberculin properly given is a specific in tuberculous affections of the glands, and that the earlier in the history of the case it is given the quicker are satisfactory results obtained. No one who, like myself, has seen chronic cases—in which, in spite of a number of operations having been performed, constant relapses have taken place—apparently cured completely by the use of tuberculin, or who has seen early cases in which the administration of tuberculin has been quickly followed by immediate and apparently permanent relief, can doubt that the efficient administration of tuberculin is to be recommended in all such cases. It must be understood that tuberculin cannot be given in any routine or haphazard fashion. To give settled doses at settled intervals without reference to the individual susceptibility and characteristics of the patient is to revert to unscientific medicine, and must, in time, bring nothing but discredit on the administrator. If the latter were the only result it would not be of much importance, but unfortunately such methods bring discredit on the profession as a whole, and make the public averse to the employment of this remedy. Tuberculin improperly given is capable of doing great harm, and not infrequently of causing death. It is imperative, when we administer this remedy, that we should have a sufficient guide to the immunising response of the blood, so that we may know the effect of our doses, what doses we are to give, and at what intervals we are to give them. In some cases we can commence with $\frac{1}{20000}$ mgrm. tuberculin T.R. by the mouth (or $\frac{1}{100000}$ under the skin), and steadily increase the dose at varying intervals to such large doses as $\frac{1}{10}$ mgrm. with nothing but benefit; in other cases we cannot increase the dose to a larger dose than, say, $\frac{1}{10000}$ mgrm. without doing more harm than good. Sir Almroth Wright, by his brilliant and fascinating work, has provided us with a guide which not only is efficient but which opens up a new era in medicine. The opsonic index is, in my opinion, capable of telling us much that we want to know with regard to the response of the blood to our doses of tuberculin. It is undoubtedly the most scientific and definite guide that we yet have. Unfortunately the laboratory technique required is difficult and laborious, and I doubt whether there are more than two dozen men in the country who are competent to perform it or to give satisfactory information to the clinician. Again, if the index is to be our guide it must be taken frequently,

certainly not less than once a day, if we are to obtain reliable information. That, of course, is an expensive business, and puts its use out of the question for the vast majority of the population. In medicine most of us have to confine ourselves to what is practical, and there can be no doubt that for the majority of patients the determination of the doses of tuberculin over a long course by means of the opsonic index is outside practical possibilities. We want a simpler guide.

For the last eighteen months I have had the advantage of being able to study, in various examples of infective disease, a large number of opsonic curves, in many of which the index was determined several times a day, side by side with the temperature curves and clinical characteristics of the cases. I have had the privilege of working with Dr. H. D. Spitta, Dr. H. W. Bayly, and Dr. H. Cockerton, and particularly, in pulmonary tuberculosis, with Dr. A. C. Inman. The work has been laborious, but it has borne good fruit. We have carried out this investigation in order to see whether any relationship existed between the opsonic index and the temperature on the one hand, and between the opsonic index and the clinical symptoms on the other. We endeavoured to use the opsonic index in such a way that we might interpret the changes of temperature, and of the clinical condition, in terms of the immunising response of the blood—in other words, we used the opsonic index as a tutor to teach us a new language. (A number of charts were shown here.) In a paper by Dr. Spitta, Dr. Inman, and myself,* and, more definitely, in a later paper on the administration of tuberculin in pulmonary tuberculosis by Dr. Inman and myself,† a real relationship between the opsonic index and the temperature and clinical condition has been shown to exist in tuberculous disease. In my experience the same relationship holds good in pneumococcic, staphylococcic, streptococcic, *Bacterium coli*, gonococcic, and *Micrococcus catarrhalis* infections. The result of this investigation is to show that it is possible to deduce the *changes of phase* in the opsonic index, and so to interpret the immunising response of the blood, without the necessity of determining the opsonic index, by a close study of the temperature curve and the clinical symptoms of a case. When the temperature rises we can deduce the fact that the opsonic index is falling; when the temperature falls we can deduce the fact that the opsonic index is rising. This is true not only of febrile temperatures but also of subnormal ones. Again, we find that an increase in the daily swing of temperature—*e.g.* 98·4° F. a.m. and 99° p.m., replaced by 97·4° a.m. and 100° p.m.—means a falling opsonic curve; whereas a diminution of the daily fluctuation—*e.g.* 97·2° F. a.m., 99° p.m., replaced by 98·4° a.m., 98·8° p.m.—means a higher level of the opsonic curve. We can therefore say that a dose of tuberculin which causes either a higher temperature or a greater swing of temperature is doing harm, and therefore is too large; whereas a dose which causes either a lowering of temperature or a diminution in the daily fluctuation —*i.e.* a "flatter" temperature—is doing good. Further, a dose which has no effect on the temperature one way or the other has no effect on the opsonic curve. Such a dose is therefore too small. (A number of charts were shown here.)

With regard to the clinical condition, we find that when the symptoms or physical signs are showing improvement the opsonic curve is raised, and that when the symptoms or physical signs are showing an extension of the disease the opsonic curve is at a lower level. An excessive dose of tuberculin in the case of glandular disease will be followed by such symptoms as a peculiar headache just above the eyebrows, restlessness, want of appetite, pain in the glands, or enlargement or temporary swelling of the glands. These symptoms are coincident with a falling index. An effective dose leads to the patient feeling better, and to an improvement in the symptoms which is coincident with a rising index.

In most cases, therefore, a close study of the temperature and the clinical symptoms enables us in tuberculin therapy, and so far as my experience goes in other forms of vaccine therapy, to obtain sufficient knowledge of the immunising response of the blood to enable us to determine our doses and the spacing of these doses, without the necessity of having resource to the laborious technique of the opsonic index. Naturally, when it is possible, it is wisest to use as many controls in any form of treatment as is practical, and if in addition we can have *frequent* determinations of the opsonic index, so much the better. In the great majority

* 'Proc. Roy. Soc. Med.,' Medical Section, April, 1908.

† 'Lancet,' October 31st, 1908.

of cases this is impracticable, and, I believe, unnecessary. When we are in difficulties, it sometimes happens that the opsonic index is a help to us and gives additional information, but on several occasions I have referred to the index as a court of appeal in cases of difficulty without obtaining any addition to the information which I had already gained from a close study of the clinical facts in terms of the index.

We may now turn to the general scheme of treatment with tuberculin. A good deal has been written on the virtues of various forms of tuberculin, and especially on the relative virtues of bovine and human tuberculin in different forms of infection. Much further work is required on this point to enable us to draw profitable conclusions. My own experience so far is that whatever the source of tuberculous infection, Koch's tuberculin T.R. is a satisfactory form to use. It can be given by the mouth or rectum or under the skin. In the case of children and in large practices or large institutions administration by the mouth has obvious advantages. A dose by the mouth is equivalent to about half the same dose when given by the hypodermic method. A dose by the mouth appears to be absorbed as accurately as when it is given by the skin, provided it is given on an *empty* stomach. It is best given in one to two ounces of tepid milk an hour before breakfast.

Suppose we have a comparatively early case of tuberculous glands without secondary infection to treat, we first adopt the general measures already mentioned, and in addition have a careful record of the temperature taken for a week before we give the first dose of tuberculin. At the end of this time we have a reasonable understanding of the case. It is a mistake to think that glandular tuberculosis is unassociated with fever, for many cases are associated with a rise to 99° F. or more at night or some other time during the twenty-four hours. In any event a temperature record is required, for even a subnormal temperature gives us most valuable information. We commence with a dose of tuberculin by the mouth which can do no harm, and then at forty-eight-hourly intervals increase it until we have produced a definite effect upon the temperature, that is, until we have lowered its level and diminished the daily fluctuation. We may commence with $\frac{1}{3000}$ mgrm. If this produces no effect, in forty-eight hours we may give $\frac{1}{4000}$ mgrm. If this has no effect we may increase the dose each forty-eight hours until we have an effect. For example, if $\frac{1}{2500}$ mgrm. leads to lowering of the temperature and to a flatter temperature it has done good. As soon as this effect wears off and the daily fluctuation resumes the same dose should be given. When this dose begins to lose its effect, or its effect lasts for a shorter time, we increase the dose to $\frac{1}{2000}$ mgrm., and so on. If any dose causes a rise of temperature it has been too large, and should not be given again for a week or so, according to the behaviour of the temperature. In most cases it is wisest then to give a somewhat smaller dose and to refrain from a further increase. In others we can repeat the same dose with benefit. We must also take advantage of the indications given by the clinical symptoms—for example, pain in a gland or swelling should make us proceed more cautiously.

Such treatment is sometimes quickly rewarded; on the other hand many months' treatment are often required. Each patient differs, and the result of treatment cannot be foreseen until the patient has been under observation for some time whilst tuberculin has been administered. Any attempt to hurry brings failure in its train. In all cases tuberculin treatment should be continued for some months after apparent recovery, in order to diminish the tendency to relapse. In many instances auto-inoculation is a valuable adjuvant. Thus in cases in which progress is slow, better results are often obtained by inducing auto-inoculation by means of a stimulating dose of X-ray exposure, or by means of a hot sand-bag.

It would, of course, take much longer than the time at my disposal to-night to deal in anything like an adequate way with the treatment of glandular tuberculosis. I have therefore refrained from going into any great detail and have dealt chiefly with principles. My main contention is that we now have in our hands efficient methods for combating this disease, provided we realise our responsibility for making a correct diagnosis at an early stage. I have also tried to show that this treatment is one that can be carried out by any careful practitioner who keeps his cases under close observation, and that the chief burden of the treatment must always remain in the hands of the clinician.

July 12th, 1909.

WITH MR. BLAND-SUTTON AT MIDDLESEX HOSPITAL.

XI.

Trauma in Relation to Malignant Tumours.

I had no thought of discussing with you the subject of trauma as a factor in producing cancer, because twenty years ago a very careful study of the writings relating to the causation of tumours, as well as a practical personal inquiry, enabled me to satisfy myself that no convincing facts were forthcoming in support of the view that direct injury led to the formation of a carcinoma. The matter has, however, become important in consequence of a recent Act of Parliament, which extends the scope of workpeople and servants injured in the course of their employment for recovering damages from their employers. As a result, cases have already been brought into courts of law for the purpose of recovering damages for malignant tumours attributed to bodily injury sustained in the course of employment, and in at least one case such a claim has been successful.

When you come to practise your profession you will quickly learn, if you have not already appreciated the fact whilst attending the out-patient rooms and wards of the hospital, that men and women almost invariably endeavour to associate a local ailment with a local cause, and this is especially true in regard to tumours of the limbs and breasts. Patients will remark sometimes in regard to an obvious tumour for which they seek advice, "I cannot account for it in any way, for I don't ever remember knocking myself there," as if it were part of their duty as a preliminary when seeking advice, to rummage their minds for a recollection of some antecedent injury.

So far as carcinoma is concerned, trauma as an ætiological factor has only been seriously advanced in the case of the breast, and it is in regard to this organ that I propose to consider the matter in detail on the present occasion.

The breast is liable to two kinds of malignant disease—carcinoma and sarcoma. The former arises in the epithelium lining the ducts and acini of the glandular elements of the breast, whilst the latter arises in its connective tissue (see Lecture II, Clinical Journal, December 23rd, 1908).

Cancer of the breast is a common disease; indeed, this organ shares with the stomach and the uterus the distinction of being the most common situations in which this disease occurs primarily. Sarcoma of the breast is an uncommon disease, and from the comparison of a number of statistical papers devoted to this matter it may be fairly stated that, out of every hundred cases of malignant disease of the breast, ninety are carcinoma and the remainder some form of sarcoma. It may also be mentioned here that these two forms of malignant disease attack the male breast. Most surgeons will agree with me in the statement that malignant disease is one hundred times more common in the breasts of women than in the breasts of men. Cancer arising concurrently in both breasts is unusual: its frequency is variously estimated by different observers at from 1 to 2 per cent. The liability of the right and left breast to become attacked by cancer is equal.

The breast, like other superficial parts of the body, is liable to injury in the form of blows, knocks and stabs, and it may be bruised when a woman falls on her breast or knocks it against hard bodies, like bedposts and the corners of furniture: it is sometimes injured by hard bodies hurled through the air, such as bricks, stones, or books. A common form of accident is a blow on the breast from an elbow in a struggle or in a crowd; brutal men inflict serious injuries on this part of women by blows with the fists, and even kicks. Street accidents constitute another common class of injury, such as being run over by vehicles, or kicked by horses. Nursemaids often complain of being thumped on the breast by unruly children, and those who are engaged in hard work receive accidental blows from broom-handles, and other forms of hand implements, or from machinery. Pressure from hard corsets has often been blamed for injuring the breasts.

In the out-patient room of a general hospital a large number of women are treated annually for injuries to the breast. When the breast is injured it bleeds like other parts of the body, and as the mammary tissues are soft the blood sometimes infiltrates them freely, producing the usual purple staining of the skin, familiarly known as a bruise. Many slight injuries of the breast, although they cause great pain (for the tenderness of the breast is proverbial), are not accompanied by any staining

of the skin, although there may be an effusion of blood in the deeper tissues.

In the majority of cases the effused blood slowly absorbs, but if much blood has been discharged into the tissues there remains, sometimes for many months, a hardened area with indefinite outlines in the tissues of the breast, and this small indurated area is sometimes supposed to be the starting-point of cancer.

It may be assumed that blows and similar severe mechanical insults to such a delicate organ as the breast, cause so much pain and leave such an impression on the mind of the sufferer that it is rarely forgotten. A definite proportion of women with cancerous breasts, which amounts to at least 10 per cent., will state unasked that they have received an injury to the breast. In some the blow occurred a few months previously, in others as much as thirty years before. A few, if closely questioned, will recall to mind an injury received some years previously.

There can be little doubt that the majority of women have received at some period of their lives a knock upon their breasts, and that the frequency with which women attribute the cause of a cancerous tumour within the breast to an injury is largely due to the belief, deeply rooted in their minds, that such injuries are the common cause of cancer, and though 10 per cent. of patients with this disease in their breast can, and do, assign a specific injury as the starting-point, it is probably true that not 1 per 1000 of women who have received a severe blow on the breast becomes the victim of cancer. With men it is different, for in them the ratio of an intensive injury as a forerunner of malignant tumours of the breast is much higher than in women, although cancer of the male breast is in the proportion of 1 to 100 in women.

It should be remembered that many lumps in the breast, supposed to be cancerous when merely examined by the eye and fingers, prove to be non-malignant when examined microscopically. Although surgeons have been looking at tumours of the breast since the days of Hippocrates, and even before that, yet to-day there is no unequivocal sign by which cancer may be recognised. In the early stages of this disease a hard, irregular, indefinitely circumscribed lump is felt in the breast, and is, as a rule, painless. In many instances the wisest and most experienced surgeons cannot be certain whether the lump is cancerous, or due to chronic inflammation of the true mammary tissue (mastitis), a tumour of the glandular tissue (a fibro-adenoma), or a dilatation of one of the ducts (a cyst), or a specific infection, such as is found in syphilis, or tubercle, and sometimes an abscess.

Age is of some assistance in the diagnosis of uncertain lumps in the breast. No undoubted case of mammary cancer has been recorded in a patient before the fifteenth year. There are very few examples recorded before the twenty-fifth year. The greatest number are met with in women between the twenty-fifth and the fiftieth years. It may occur at any age after fifty, and has been observed in a woman, ninety years of age.

Although absolute ignorance prevails concerning the cause of cancer, few pathologists who have given special attention to the matter will admit that physical injury to a part can cause it to become cancerous.

The details of an actual case will serve to show how necessary it is to carefully follow up patients in order to avoid a false impression. In 1906 I removed the left breast of a married but childless woman on account of carcinoma; the axillary fat and lymph-glands were also removed. The patient made an uneventful recovery. The cancerous nature of the disease was established by a careful microscopical examination of the breast and the lymph-glands. In 1909 this woman again came under observation with a rounded lump in the right breast, which she attributed to a blow from a corner of a box which she received, four months previously, whilst struggling with another woman for the possession of the box. The lump in the breast was as big as a tennis ball, hard, and somewhat adherent to the skin. The nipple appeared to be normal. The condition of the tumour and its relation to the breast were quite unlike primary cancer, but resembled in many points secondary carcinoma of the breast, for I must point out to you that when the mammary gland is the seat of secondary cancer the disease assumes the massive form which is so often seen in metastatic cancer. In its clinical features the tumour resembled a mammary sarcoma, and the rapid growth following injury led me to entertain the idea that this lump might prove to be sarcomatous. There was no doubt as to the advisability of removing the breast,

and in the course of the operation it proved to be a cyst with unusually thick walls.

Sarcoma of the breast.—It has already been mentioned that sarcomata are unusual tumours in the breast, and that they constitute about 10 per cent. of the malignant tumours of this organ. Among recent statistics on this point may be mentioned those of Poulsen (Copenhagen): Among 335 tumours of the female breast 33 were sarcomata; and Gebele among 359 mammary tumours in Bergmann's klinik found 34 sarcomata. Schmidt found in 139 cases of malignant disease of the breast 126 examples of carcinoma and 13 of sarcomata. Horner among 172 malignant tumours of the breast found 14 sarcomata. Sarcoma occurs at an earlier age than cancer, and women are most liable to this form of malignant disease between the twentieth and fortieth years of life, whereas cancer is most frequent between the thirty-fifth and fiftieth years.

As with cancer, the patients often attribute the disease to an injury, especially to what may be called an "intensive injury." For example, a constable was kicked in the breast; about two months later he noticed a small lump at the seat of injury; this quickly increased and proved to be a sarcoma (Harrison Cripps).

A spinster, æt. 50 years, employed as a cook, "let a round of beef fall on her breast;" it gave her a severe blow. A month later she noticed a small hard lump which gradually increased in size, and in two months it was as big as a penny. It then grew and formed a large tumour. The breast was freely removed, the disease quickly recurred, and the patient died within fifteen months of receiving the blow (Sir George Thomas Beatson).

A married woman, æt. 58 years, received a blow on the right breast; four months later she came under observation with a tumour in the breast which grew quickly; six weeks later it had grown to the size of a child's head. It was removed and proved to be a round-celled sarcoma. She returned four months later with a recurrence, and died within a year of receiving the injury (Schmidt).

Such clear and definite cases of injury being followed by a sarcoma as in the three preceding reports are certainly uncommon in the breast, but they are frequent in the limbs, especially in children and adolescents. There would be no difficulty in collecting a score of examples from current surgical literature. The following case came under the writer's notice: A man, æt. 21 years, received a blow on the shin from a barrow loaded with bricks. One month later a swelling was noticed, and proved to be a round-celled sarcoma of the tibia as big as a cocoa-nut. Amputation was performed (Museum, Middlesex Hospital).

Every pathological museum of any pretentions contains specimens of sarcomata growing in bones of the head and the limbs as a sequel to a severe single physical injury. Such cases are by no means confined to the civilised inhabitants of the globe. A girl, æt. 16 years, a native of the Island of Mabuiag in Torres Straits "fell down and hurt her knee but did not break the skin." Shortly after this the knee began to swell, and in three months she came under the care of Dr. G. V. White, in Thursday Island, and the leg was amputated. The girl died two months after her return to Mabuiag. Professor Allen, of Melbourne, examined the growth and found it to be a *periosteal* sarcoma ('Third Scientific Report of the Imperial Cancer Research Fund').

In the case of sarcomata we are met with similar facts to those surrounding the relation of trauma to the incidence of cancers (carcinomata), namely, that surgeons see very many patients with sarcomata who cannot recall any preceding injury to the part; and of the enormous number of contusions and injuries only an infinitesimal proportion is followed by sarcomata. Small as is this number, the circumstances relating to the sequences are such as to lead surgeons to believe *that a single "intensive" injury may occasionally induce the growth of a sarcomatous tumour*, and to place it outside the category of mere coincidence.

The attitude of surgeons as reflected in their writings concerning the influence of trauma, or physical insults, as an ætiological factor in the production of malignant tumours in the breast, justifies the following statement:

In regard to cancer (carcinoma) all surgeons of experience admit that there is a definite history of intensive mechanical injury in about 10 per cent. of the patients. They are very careful not to express a definite opinion as to the causal relationship of such injuries to the formation of cancer in the breast. There is also a paucity of published statements from surgeons of great experience affirming trauma as a cause of mammary cancer.

In regard to sarcoma of the breast, there is a definite opinion held by experienced surgeons to the effect that there are many carefully observed and thoroughly reported cases in which primary sarcoma of the breast has quickly supervened on a single intensive injury. The sarcomatous nature of such tumours has been ascertained by a microscopic examination at the hands of a competent pathologist, and their malignant nature has been confirmed by the early death of the individual. It is undeniable that a single intensive blow or knock on the breast may be occasionally followed by a sarcomatous tumour.

There is, however, a wide diversity of opinion as to the exact conditions under which any given case of tumour is to be regarded as of traumatic origin. All agree that the situation of the tumour must correspond to the site of the injury, but there is no definite agreement among surgeons as to how long an interval may elapse between the injury and the appearance of the tumour in order that they may be regarded as cause and effect. This can only be decided by a careful study of individual cases.

In relation to this subject it is necessary to mention that of all the tumours, benign or malign, which attack man, sarcomata are the most difficult, from the clinical and histological points of view, to distinguish from a simple inflammatory, or from an infective swelling.

It is undesirable to conclude this lecture on trauma in relation to cancer and sarcoma without referring to a class of tumour directly depending on injury. I refer to those interesting cysts met with chiefly on the fingers, the cornea, and iris, due to the accidental embedding or implanting of minute portions of cutaneous epithelium. These "implantation cysts," as I ventured to name them some years ago, appear chiefly on the volar surface of the fingers, and vary in size from a split-pea to a cherry (Fig. 1). These cysts lie in the loose tissue of the skin, and if the skin which covers them is carefully examined you will, as a rule, find a scar. Careful accounts of these cysts were published many years ago by Le Fort (1881) and Polaillon (1884). These surgeons recognised that such cysts were due to small fragments of skin, sometimes containing hair-follicles and sweat-glands, which have been carried into the subcutaneous tissue by a penetrating foreign body. This implanted skin becomes encapsuled by connective tissue and develops into a cyst.

Accidents which lead to the formation of such cysts occur in a variety of ways, such as punctures by awls, forks, needles, thorns, glass, knives, bites, lacerations, and incisions made in the course of surgical operations, and by shot.

When such a cyst is examined microscopically, especially one from the pulp of the finger, "it appears as if a piece of skin had been inverted." In others the implanted epidermis appears to be shed in layers, and thus produces a laminated appearance; in one instance the cyst contained a fragment of a bullet. Wieman has twice found foreign bodies in implantation cysts.

The belief that these cysts arise from fragments of the epidermis accidentally implanted into the subcutaneous tissue is confirmed by what we know of similar cysts on the iris and cornea associated with mechanical injury. Hulke (1869) studied the microscopic features of certain small cysts occasionally found on the iris, and found that some of them contained sebaceous material, such as fills the cavities of dermoids; he stated that in a large proportion of cases there was a distinct history of antecedent mechanical history, and he suggested that some of these cysts originated from portions of Descemet's membrane torn from the cornea and implanted on the iris. Many instances are now known in which eyelashes have been implanted on the iris by foreign bodies, such as knives, forks, needles, foils and the like penetrating the cornea. Even so gross a weapon as a sword has brought about such an event, as in the case of Barry Sullivan. This actor was playing in Shakespeare's famous tragedy, "Richard III," and in Act v, scene iv, in which is represented the combat between Richard and Richmond, some spirited sword-fighting occurs. In this encounter Barry Sullivan received an accidental perforating wound in the eye. Later a cyst containing an eyelash grew from his iris (see Treacher Collins, 'The Anatomy and Pathology of the Eye,' 1896).

FIG. 1.—An implantation cyst in the skin of the finger.

Similar implantation cysts occur in the cornea after gunshot injuries, blows from tip-cats, and in the lines of incisions made for the extraction of cataracts, etc.

I have drawn your attention to this matter as a prelude to some interesting pathological processes which occasionally occur in the abdomen as sequelæ to mechanical injuries of ovarian cysts. When a woman has a large ovarian cyst one of the dangers she runs is rupture of the cyst from violence: for example, a cyst of this kind has been burst during an "immoderate fit of laughter"; in

stooping to button the boots; during manipulation by a physician; during vomiting or coughing. A common cause is a fall, either from a chair, a carriage, or in alighting from a gig. When the cyst contains clear fluid it is quickly absorbed and excreted as urine. In the case of a purulent cyst it would probably have a fatal termination. When the tumour is a dermoid (embryoma), the grease, hair, and epithelial cells it contains are scattered over the abdominal viscera, the cells become engrafted on the peritoneum, and in some instances hundreds of minute dots, each furnished with a tuft of hair, have been found. Occasionally these bodies are pedunculated and form cysts as big as bantam eggs. In the majority of such cases there was distinct history of mechanical injury. The relation of these nodules to the peritoneum is different to what is found where secondary nodules of cancer grow in relation with this serous membrane. The cells from dermoids engraft themselves on, but do not penetrate, the peritoneum, but in the case of the cancer-cells this membrane is eroded and penetrated by them, the cells exhibiting the same invasive property so characteristic of them in other situations; but even cancer-cells may have their invasive property inhibited by the extraordinary encysting power possessed by the peritoneum. It has long been known that when aseptic foreign bodies are introduced, or find their way into the general peritoneal cavity they become quickly coated with an exudate (for convenience we call it "lymph"), which quickly organises and forms a fibrous capsule. This capsule is known as a cyst. Collections of fluid, such as blood and serum, are often encysted in this way. An interesting condition is often found when a papillomatous cyst of the paroöphoron bursts and scatters its cell-containing fluid far and wide in the belly. These cells become engrafted and grow into warts, and in some cases I have found warts or papillomata produced under these conditions contained in definite, complete, and independent cysts. Nowhere in the body can cyst-production of this kind be studied so completely as in the belly, but it assists us in appreciating the fact that the iris, the cornea, and the subcutaneous tissue generally, possess the power of throwing a capsule around intruding epithelium.

I have dealt with these matters in connection with trauma in relation to tumours because, in the present condition of the law, cases are bound to arise in which your opinions will be sought in regard to the effects of injuries on pre-existing cysts and tumours, as well as on the debatable question of trauma as an ætiological factor in causing malignant disease. In such matters the old adage applies, "To be forewarned is to be forearmed," and, as some of you will quickly learn, lawyers are often cunning men.

July 12th, 1909.

SOME POINTS IN THE SURGICAL TREATMENT OF FRACTURE OF THE BASE OF THE SKULL.*

By L. B. RAWLING, M.B., F.R.C.S.Eng.,

AND DISCUSSION THEREON BY

MR. GORDON WATSON AND MR. T. H. KELLOCK.

MR. PRESIDENT AND GENTLEMEN,—The title chosen for the subject this evening is rather misleading, for a fracture of the base of the skull requires in itself no treatment. The mortality is about 50 per cent., death resulting either from associated injury to intra-cranial contents or from the remote development of meningitis, the infection arising from the communication of the fracture with the aural, nasal or naso-pharyngeal spaces. The title has, however, been chosen because I wish to confine my remarks mainly to these cases of fracture which, though associated with intra-cranial injury, yet offer no marked localising features aiding in the diagnosis as to the site of the lesion.

I do not propose to allude to the indications for operation, or to the operative procedures necessary, when the fracture is complicated by the presence of localised extra- or subdural hæmorrhages. When such conditions are evident, I conclude that there will be no question as to the necessity of operating at the earliest possible moment. Such measures offer the only hope of recovery, not only of a post-operative return to mental and bodily faculty, with apparent restoration to health, but also of immunity in the future from the later complications of head-injuries in general, namely, headache, epilepsy, insanity, etc.

It will also, I think, be granted that the classical pictures of middle meningeal hæmorrhage and of localised subdural extravasations are seldom forthcoming. Such hæmorrhages are usually accompanied by contusion or laceration of the brain, with the inevitable result that localising features are obscured at an early period by those symptoms which are regarded as exemplifying the clinical conditions of concussion, irritation, and compression of the brain. The average case, therefore, of fracture of the base of the skull evidences the conditions present:

* Delivered before the Medical Society of London.

(*a*) By certain symptoms pointing to the nature and site of the lesion, external hæmorrhages, nerve palsies, escape of cerebro-spinal fluid, etc.

(*b*) By other symptoms pointing to the presence of injury to the intra-cranial contents.

Before, however, dealing with the main matter of my subject, the treatment of the average case of fracture of the base of the skull, I wish to devote a few minutes to the consideration of profuse and continuous bleeding from the ear, its cause and treatment.

In 1842 Chassaignac reported the case of a man who fell down an area and sustained a severe head-injury. For two days the man was confined to bed suffering from severe aural hæmorrhage. On the third day, feeling tired of confinement, he got up and walked some distance, on a cold and frosty day, to seek further advice. Whilst returning home he complained of headache, and noticed that the bleeding from the ear had ceased. He went to bed, soon became unconscious, and died the next day. The post-mortem examination revealed an extensive extra-dural extravasation of blood, derived from a torn lateral sinus and an injured middle meningeal artery. The petrous bone was also extensively comminuted. By piecing together the various points in the case we are able to picture the course of events. The extra-dural blood during the first two days of the illness was able to escape from the auditory meatus by means of the passage afforded through the comminuted petrous bone, but, as a result of the cold atmosphere, the blood clotted in the external auditory meatus, the extra-dural extravasation was dammed within the skull, compression symptoms supervened, and the patient died.

The lessons to be learnt from this case apparently escaped attention, and the conditions were certainly not appreciated by me till the year 1903, when a man was admitted under my care suffering from profuse hamorrhage from the ear. This continued till death supervened, fourteen hours later. The autopsy revealed an extensive extra-dural hæmorrhage from a torn middle meningeal artery and comminution of the roof of the middle ear with laceration of the tympanic membrane. This case was reported in my Hunterian lectures on fracture of the base of the skull in 1904. The diagnostic value of this symptom was subsequently carefully borne in mind, with the result that I was enabled to come to the following conclusions:

(1) That profuse and continuous hæmorrhage from the external auditory meatus suggests the probability that the surgeon has to deal with a case in which there is an extra-dural extravasation and an extensive fracture of the petrous bone, probably involving the tegmen.

(2) That plugging of the external auditory meatus is to be condemned, insomuch as the free escape of blood is the one factor that prevents cerebral compression.

(3) That operative measures for the relief of the extravasation are to be seriously taken into consideration, even in the absence of all the classical symptoms of middle meningeal hæmorrhage.

(4) That syringing of the ear is absolutely contra-indicated on the ground that the lacerated tympanic membrane and comminuted tegmen tympani expose the patient to grave risk of meningeal infection.

On many occasions I have carried out operative procedures, guided by this symptom alone, and, though the conditions alluded to have not always been found, yet success has been sufficiently frequent to convince me that my deductions are correct.

The source of the hæmorrhage is variable. The blood may be either arterial or venous. In the latter case it is usually derived from a torn lateral sinus. Such a case was recorded by Milligan in the 'Transactions of the Otological Society' (vol. viii, p. 69). The blood is, however, usually arterial, and derived either from a rather constant branch of the posterior division of the middle meningeal artery that crosses the roof of the middle ear or from the main vessel itself, for it must always be borne in mind that the basic fracture is generally prolonged in the upward direction, towards the vertex of the skull, the meningeal artery being injured as it crosses the line of fracture.

This particular fracture to which I allude is of such frequent occurrence, and the relation to the tegmen tympani and other parts of the petrous bone is so constant, that I have named it "the typical fracture of the base of the skull." With your permission I will show you photographs taken from specimens in my own possession and of others presented by me to the museum of the Royal College of Surgeons.

When the skull is examined as a whole, it will be

seen that the fracture passes across the roof of the middle ear and along the suture between the petrous portion of the temporal bone and the great wing of the sphenoid, in the direction of the sphenoidal body. The exact relation of the fracture to the auditory and neighbouring regions is preferably investigated by examining the anterior aspect of the posterior fragment, that is to say by examining that part of the temporal bone which lies immediately behind the line of fracture. From without inwards the following structures will be exposed: the posterior two thirds of the external auditory meatus, the lacerated tympanic membrane, and the greater part of the middle ear with contained ossicles. Above you will see the aditus and antrum and mastoid cells, in front, the Eustachian passage and internal carotid artery, whilst in many cases it will be seen that the fracture exposes the geniculate ganglion of the facial nerve. The illustrations will evidence the parts exposed and involved in the line of fracture. The specimens also illustrate well my earlier remarks with regard to the ready escape of blood to the exterior and the dangers arising from injections of fluid through the external auditory meatus.

I will now return to the main part of my subject, the treatment of the average case of fracture of the base of the skull.

The question as to desirability of undertaking operative procedures naturally hinges on a general examination of the patient, but, just as in appendicitis, the surgeon, in deciding as to the necessity of operative treatment, is guided largely by the character of pulse, so in these cases I regard the temperature as the main factor enabling one to adopt a definite line of procedure, operative or non-operative.

After investigating a large number of cases, about 300 in all, during the past six years, I was enabled to classify the cases into three groups:

(1) Where the temperature rises steadily and progressively to 103° F. or more, the reaction from the primary collapse stage being of a marked and forcible nature, and the patient dying with definite evidence of cerebral compression.

(2) Where the temperature rises to 100–102° F. and there "marks time." This is the "crisis" of the case, a further rise or fall indicating respectively a fatal or favourable termination.

(3) Where the temperature remains subnormal, the patient remaining in a condition of severe cerebral shock and usually dying within a few hours.

With this temperature chart as a guide one is able to formulate certain rules with regard to the treatment appropriate to each individual case.

Treatment of cases that fall under Group 3.—The patient is in a condition of severe cerebral shock, due, in the majority of cases, to contusion or laceration of the brain, the grosser lesion being most commonly situated either at the apex of the temporo-sphenoidal lobe or at the anterior inferior part of the frontal pole. The patient is, however, suffering from shock, and the treatment advocated for that condition in general is equally applicable to these cases in particular. The patient should be placed in the so-called head-down position, and the extremities firmly bandaged from below upwards. The vaso-motor depression should be combated by the administration of rectal or intra-venous infusions of saline solution, to each pint of which is added one drachm of a 1 in 1000 solution of adrenalin chloride. It is at once obvious that, whilst combating the condition of shock, this mode of treatment will at the same time tend to encourage fresh hæmorrhage within the skull if the brain should have been lacerated or if intra-cranial vessels should have been torn. For this reason I regard rectal infusion as the safer of the two methods and look upon it as the method of choice, in spite of the fact that intra-venous infusions bring about a more rapid alteration in the patient's condition. The effect of the infusion must be watched with the greatest care, and as soon as the temperature shows a tendency to rise, say from the subnormal to the normal, the infusion process must be stopped and the further progress of the case carefully observed.

The risks attendant on this mode of treatment are obvious, but in their estimation it must also be borne in mind that if the patient remains in the collapsed stage without evidencing any sign of reaction he is practically certain to die. If the treatment advocated should tide the patient over the collapse stage and induce a definite reaction, as exemplified by the rise in temperature, the further treatment of the case can be considered under Groups 1 and 2.

Treatment of cases that fall under Groups 1 and 2.—In Group 1 the progressive rise in temperature is usually associated with symptoms pointing to compression of the brain, a slow pulse, noisy and stertorous respiration, hot skin and turgid face. Later on, as a result of the increasing pressure, the medullary centres begin to show signs of exhaustion, the pulse-rate increases and the respiration becomes Cheyne-Stokes' in character.

Whether these symptoms result primarily from the nature of the lesion or secondarily after the adoption of those measures advocated for the collapse stage it matters not. Our indications with regard to the correct treatment are urgent and clear. The increasing intra-cranial pressure must be reduced. This desideratum is carried out preferably by the ligature of a bleeding meningeal artery or by the occlusion of a torn venous sinus, but, unfortunately, such a course is frequently out of the question. We have therefore to deal with an increased and an increasing intra-cranial pressure, without definite localising symptoms, and for this condition we have at our disposal the following measures: venesection, lumbar puncture, and "decompression" operations.

Venesection.—I regard venesection as a valuable means of reducing the increased intra-cranial pressure. It is mainly of use in those cases that hover between what one may call early or slight compression and the fully developed condition. Venesection may therefore be regarded as of especial advantage in those cases that fall under Group 2. The bleeding should be carried out after exposure of the median basilic, external jugular or internal saphenous veins, preferably from the first-named site. The amount of blood to be withdrawn varies according to the individual and according to the circumstances of the case, but in general the escape of blood should be continued till the pulse becomes frequent, soft and compressible. The operation not infrequently turns the scale in favour of the patient. Venesection may also be carried out in combination with "decompression" operations, that is to say, in those cases that fall under Group 1.

Venesection, when applied to suitable cases and carried out with judgment, affords valuable help in tiding the patient over the period of crisis previously alluded to. The most careful observation is needed in estimating the quantity of blood to be withdrawn, the pulse, the temperature, and the general condition of the patient affording an adequate guide.

"Decompression" operations.—"Decompression" operations may be carried out over the cerebellar fossa or over the temporal region of the skull. In cerebellar decompression a suitable scalp-flap is turned down and the trephine applied over the centre of the exposed occipital bone. After the removal of the disc of bone, the walls of the cerebellar fossa are freely cut away with the craniectomy forceps up to the line of the lateral sinus above, to the mastoid process in front, to the vicinity of the foramen magnum below, and almost up to the middle line on the inner side. The bulging dura mater is incised in a crucial manner, right up to the margins of the osseous gap. All meningeal vessels that cross the line proposed for dural section are first ligatured by being under-run with a fully curved needle threaded with fine catgut. A small drainage-tube is inserted between the dura and the cerebellum and brought out through the most dependent part of the scalp-flap. The flap is then carefully sutured in position. The tube remains for twenty-four hours or more according to the circumstances of the case. I have carried out this operation on several occasions, and though the immediate results are good, the more remote are by no means satisfactory.

The temporal operation, more correctly known as the "intermusculo-temporal" operation of Harvey Cushing, often brings about the most satisfactory results. Before dealing with the technique of the operation, it will be convenient to enumerate the advantages of the operation as claimed by the originator:

(*a*) The frequency with which the bony lesion occurs in the middle fossa of the skull.

(*b*) The fact that cerebral contusions are especially liable to involve the tip of the temporo-sphenoidal lobe.

(*c*) The exposure of the meningeal territory, and the ease of determining the presence of an extra-dural hæmorrhage.

(*d*) The possibility of draining through a split muscle rather than directly through the scalp.

(*e*) The subsequent protective action of the muscle in case a hernia tends to form in consequence of traumatic œdema.

(*f*) The subsequent absence of any deformity, the skin incision being carried out in the main through the hairy part of the scalp.

The intermusculo-temporal method of cerebral decompression is carried out as follows: After sterilisation of the scalp a large piece of gauze is thrown over the head, maintained in position by the scalp-tourniquet, to which allusion will be made presently. The skin incision starts behind the external angular frontal process, curves upwards and backwards along the temporal crest, and curves down to a point immediately in front of the tragus of the ear. The incision is carried through the skin and subcutaneous tissues only, and the flap turned down towards the level of the zygoma. The flap should include the superficial temporal vessels, care being taken not to injure the artery at the base of the flap. The temporal muscle and fascia are then divided in the direction of their fibres down to the bone, from the centre of the temporal crest to the mid-

point of the zygoma, the muscle-fibres being stripped away from the bone in the forward and backward directions, and retracted to their uttermost limit. Care must be taken not to detach the muscle from the region of the temporal crest. The trephine is applied over the bone in the angle between the course of the anterior and posterior branches of the middle meningeal artery. The disc of bone is removed, and the dura mater carefully separated from the overlying bone in all directions. The craniectomy forceps are then utilised to cut away the bone entering into the formation of the temporal fossa of the skull, especially in the anterior and posterior directions. The bulging dura mater is crucially incised, all meningeal vessels that cross the line proposed for dural section being first under-run in the manner previously described. These dural incisions are carried right up to the margins of the osseous gap. The four dural flaps are turned outwards, and the antero-external aspect of the temporo-sphenoidal lobe exposed. A drainage-tube can now be inserted along the floor of the middle fossa of the skull in the immediate vicinity of any lacerated brain that may be present. The dural flaps are allowed to lie loosely over the surface of the brain, and the drainage-tube is brought out between the fibres of the temporal muscle, this muscle being elsewhere carefully sutured with catgut. A suitable hole is cut through the skin-flap and the flap sutured in position. The tube is allowed to remain for twenty-four hours or more, according to the circumstances of the case.

In all head operations it is essential that the operative procedures should be completed with the utmost expedition and with all possible precaution against undue bleeding. Hæmorrhage may be completely controlled in this operation by the use of the scalp-tourniquet and by the underrunning exposed meningeal vessels. The scalp-tourniquet is fashioned after the style of Esmarch's tourniquet, and is applied in the following manner: It is passed round the head so as to lie in front immediately above the supra-orbital margin, laterally it crosses or lies above the ears, and then passes round the lower occipital region. As the tourniquet is tightened up there is a tendency for it to slip down over the eyes. This is prevented by a median tape which passes over the head from nasion to below the union, acting casually as a convenient guide to the surface-marking of the superior longitudinal sinus. The vessels controlled are the frontal, supra-orbital, temporal, and occipital. When the scalp-tourniquet is correctly applied there is no hæmorrhage from scalp vessels, and the surgeon is enabled to proceed with the trephining immediately after the formation of the scalp-flap, much valuable time being saved as there is none of that troublesome clamping and ligaturing of scalp vessels—a conspicuous feature under ordinary circumstances. The amount of blood lost is very slight, and the shock of the operation correspondingly diminished.

I am accustomed to use the tourniquet on all available occasions, and cannot speak too highly in its favour.

The operation of intermusculo-temporal cerebral decompression may be carried out on one or on both sides of the head; if on one side only, preferably on that side on which the laceration is present. In connection with this, it may be wise to add that laceration by *contrecoup* is more common than direct laceration. Consequently, in cases of doubt the operation should be conducted on the side of the head opposite to that at which the injury was received.

With regard to *lumbar puncture*, I do not look upon this method as of any use in the treatment of injuries to the head. From a diagnostic point of view the presence of blood in the cerebro-spinal fluid, as withdrawn by lumbar puncture, suggests the presence of intra-dural hæmorrhage, nothing more. I have never seen the slightest benefit result from this mode of treatment.

Before I conclude I should like to say a few words with regard to the treatment of subdural hæmorrhage. The trephine is applied over the suspected region, the disc of bone removed, the dura crucially incised, and the clot exposed. Free drainage is essential, and this must be supplied from the most dependent part of the clot. For this purpose the bone must be cut away, either with Horsley's gouge or other craniectomy forceps, to the lower limit of the clot or to within a short distance of the base of the skull. The channel so made need not be more than three quarters of an inch in breadth. The dura is incised along the middle of this channel, from the trephine hole above to the bone below. Sutures are passed through the apex of each of the four dural flaps above, and through the edges of the downward prolongation of the dural incision as required. By gentle traction the margins of the dura mater are turned outwards, and the clot exposed from top to bottom. It is usually quite impossible to remove the whole of the clot, but much may be scooped away with a spoon and washed away by means of irrigation. A drainage-tube is inserted beneath the dura, at the most dependent point, and the membrane elsewhere sewn up in the manner depicted in the illustration. The tube is brought out through the scalp-flap, and this flap then sutured in position with a few salmon-gut sutures.

Mr. Gordon Watson said that as it was his lot to make many post-mortem examinations at St. Bartholomew's on cases of fracture of the skull, any measures which would diminish the number of such cases would be welcomed. The cases of the kind which one saw in the post-mortem room

seemed to die either from laceration of the brain or from sepsis. The latter lived perhaps a week or more, and then their death was due to meningitis. Those cases were beyond the reach of operation. In the majority of cases which died of laceration of the brain, the chief laceration was on the side opposite to that on which the impact was received; often the laceration was on both sides. He, like the author, had frequently noticed that the chief injury was on the other side. With regard to decompression, it would be interesting to know if Mr. Rawling could tell of cases where he had first treated the cerebral shock with rectal saline, and subsequently treated cases by relieving the compression induced by infusion of saline *per rectum*. He could not speak from experience of that treatment, but it seemed to be difficult to know when to stop the one and begin the other. He hoped that at some future time Mr. Rawling would be able to give some figures showing the results of his improved technique with regard to hernia of the brain after trephining, because the splitting of the temporal muscle was a very great advance.

Mr. T. H. KELLOCK asked whether the temperatures which had been shown were morning and evening or taken at shorter intervals. Mr. Rawling said that in the cases which he classed as Group 1, where there was constant high temperature and in which death occurred almost immediately after the accident, this was due to compression. He (Mr. Kellock) was reminded of those cases in which the nervous system was interfered with by operation, especially in children, for such conditions as meningocele and spina bifida. The patients sometimes died within twenty-four or thirty-six hours of the operation, with high temperature, but without signs of sepsis, in fact too soon for the latter to have been fatal. In those cases death was possibly due to traumatic meningitis, which spread to the brain. And he had wondered whether in the group of cases which Mr. Rawling described as dying rapidly after the receipt of the injury, the high temperature might be analogous to that in those cases. He asked Mr. Rawling whether he could explain the much better present-day prognosis of cases of fracture of the base of the skull compared with that obtaining only comparatively recently. It used to be considered that a case of fracture of the base was almost inevitably fatal. Now, however, the cases were not looked upon with the same terror. They were treated now on the same lines yet they did not now seem so certain to die. He thought much of the improvement was due to what Mr. Rawling had just said, that syringing out of the ears when there was excessive hæmorrhage was a dangerous proceeding; for the same reason plugging was dangerous. To try to keep the blood in when it was trying to make its way out was mistaken treatment. Moreover, the syringing sometimes being in the hands of people not very skilful added to the danger. That seemed to be the only difference in the modern treatment of the condition, yet the results were much better. He had also been glad to hear Mr. Rawling's disapproval of lumbar puncture, which was looked upon as a remedy for so many ills of the brain and spinal cord.

Mr. RAWLING, in reply, said that he was firmly convinced of the accuracy of Mr. Gordon Watson's remarks about laceration of the brain, it was a point he demonstrated in his Hunterian lectures that laceration of the brain was often more severe on the side opposite to that at which the injury was received. That fact could not be too carefully borne in mind in operating for compression. He quite saw Mr. Gordon Watson's point with regard to the difficulties appertaining to the question as to those cases which required treatment by infusion and those in which operative measures were indicated. In this, however, he was largely guided by the temperature charts. These charts had been worked out after some years' careful observation, and the three groups were sharply demarcated from one another. In the first group there was a marked and progressive rise of temperature, and nearly all the cases died. In the second group the temperature remained subnormal, and most of these cases died also. In the intermediate group the patient reacted to a certain stage, and then came the crisis of the case. With such a chart in one's mind one could picture the course of events.

In the collapse stage the patient was suffering from nothing more or less than severe cerebral shock, a condition which should be treated after the general principles of surgical shock.

In answer to Mr. Kellock, he stated that the rise of temperature was progressive, rapidly rising from 96° to 105° F. or more, and there was no tendency for the temperature to fall immediately previous to death. Quite the reverse was the case, the temperature often rising another degree or two within half-an-hour after death. What the temperature changes are due to is quite another question. Laceration was usually present, but not necessarily so; frequently there was nothing to show to account for the changes. With regard to the prognosis one must always be very guarded, for though one could usually foretell the early prognosis by a glance at the temperature chart, yet the ultimate prognosis was very difficult to determine. If the intra-cranial pressure was relieved the outlook was much improved, and it was highly probable that the mortality would be reduced in the near future by carrying out suitable operative measures in selected cases.

He was glad to hear Mr. Kellock's remarks with regard to the futility of lumbar puncture.

July 12th, 1909.

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** Specially reported for the Clinical Journal. Revised by the Author.*

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A CLINICAL LECTURE

ON

OBSTRUCTION OF THE LARGE INTESTINE.

Delivered at St. Bartholomew's Hospital.

By ANTHONY A. BOWLBY, C.M.G., F.R.C.S.,
Surgeon to the Hospital.

GENTLEMEN,—I propose to speak to you to-day about obstruction of the large intestine. The case which I take as my text is that of a man, æt. 62 years, who is at present in Darker Ward, and came in ten days since. Two and a half years ago he began to notice a sense of fulness in the bowel on defæcation. He found later on that he did not appear to completely empty his rectum. It did not cause him much discomfort or alarm, and after that he had attacks of constipation, which appeared to alternate with attacks of looseness of the bowels, the latter being largely due to the fact that he had from time to time to take aperient medicine. A year ago he noticed that at each stool he was liable to pass mucus, and he said to me that the fæces he passed were about the consistence of paint. But he had never passed for some months a really solid, formed motion. He then began to lose weight, and his abdomen became habitually more and more distended. So when he was sent to the hospital one day last week the doctor wrote to say that he was sending a patient whom he believed had complete obstruction, and required an operation. When we came to examine him we found his abdomen was enormously distended, and at the same time he did not appear to be in such pain as you might expect from its size, and he said he had not been sick at all. I tried to persuade him to come into the hospital at once, explaining that an operation was urgently necessary. But he was so used to a distended abdomen, and I

suppose had so often had attacks of constipation and subsequent diarrhœa before, that I could not persuade him to come in. He went away, and I wrote to his doctor to say that I considered the patient was in danger on account of the distension of the bowel, and asked him to go and urge him to come back to the hospital next day. In this way we persuaded him to come back, and by the next day he was feeling worse. He came in in the evening, and was taken down to the theatre to have the operation of colotomy done, and whilst he was on the stretcher and about to have his anæsthetic he was taken with intense abdominal pain. The administration of the anæsthetic was continued, and within five minutes of his having this violent attack of pain I had opened the abdomen. I found his peritoneal cavity contained a good deal of free gas, so it was evident that the bowel had begun to give way. At the same time it was satisfactory to notice that there was nothing in the way of fæcal matter inside the abdomen, and no fluid or solid particles. We drew up the sigmoid flexure, opened it, put a tube in, and rapidly drained it. When this had been done I felt inside the abdomen with my hand, and found not only a distension of the whole large and small intestine, but an enormous distention of the cæcum. From that time onwards the man has improved, and all one can say at present is that the distension has now gradually passed away, and that he has a colotomy wound which is in process of healing. That is a typical case of long-standing obstruction of the large intestine, which dates from two and a half years ago. You might be tempted at first to think that a man who has had difficulty with his bowels for as long as that is not likely to have cancer. But one of the noticeable things about cancers of the rectum is the very long time that some of them last. I can tell you of another case, a man who came in here with intestinal obstruction many years ago, on whom colotomy was performed and in whom no cause for the obstruction was discovered. He went away with his colotomy wound still open, and continued to pass all his motions by this new aperture. Four and a-half years afterwards he came back on account of not being so well, and then it was found that he had a large cancerous growth near the brim of the pelvis, and there could be no doubt that he had had this cancerous growth for all those four and a half years, and of course he must have had it before that time, because when he first came to the hospital it had already advanced sufficiently to cause obstruction, and in another case where I had to do with a patient who had carcinoma of the cæcum, he was known to have had a lump in his cæcum at least seven years before it came to be excised. That shows that in a certain number of cases, unfortunately only a small proportion of the whole number, of cancer of the rectum there is a very slow growth of the tumour.

Another question is, What is the mere mechanical effect of any increasing obstruction of the rectum or colon? What is the effect on the wall of the bowel of an obstruction, which may be due to any cause besides cancer?

In the first place there is an hypertrophy of the muscular coat, but coincidently with this there is a dilatation of the lumen of the bowel by the retained gas and fluid. As time goes on the over-stretching becomes more marked, and, as the muscle-fibres separate or even tear, the mucous membrane at these places is only supported by the peritoneum.

The mucous membrane, of course, is not sufficiently strong to withstand any tension. And besides that, in these cases it is always weakened by the formation of numerous small ulcers, which are the result of this extreme stretching of its coats and the interference with their proper nutrition. Here is a portion of the cæcum of a man in whom these events had occurred. He had gone on for a long time, for months and even years, with gradually increasing obstruction, and finally he had complete obstruction. The muscular coat in this specimen has given way and the peritoneum has begun to split, and in this case the whole of the colon as well has ulcerated. One of these ulcers has given way at a spot where the peritoneum has split, and the contents of the cæcum were discharged into the peritoneal cavity. The bowel burst. That is an uncommon thing, because in very many cases before that happens—long before it happens—the patient gets too ill to continue to live with this increased distension, and he dies as a result of it and of his sickness, and his inability to take food; and death, therefore, supervenes before all these changes which I have referred to have had time to run their course. You will remember that in the case of the man of whom I

spoke first, and upon whom we operated the other day, a sudden intense pain occurred whilst he was being prepared for operation. I have no doubt myself that what happened was that the peritoneal coat of the cæcum had split, and that one of these little ulcers gave way and allowed the gas which we found to escape into his peritoneum, but fortunately for him, before the rent had had time to increase in size his sigmoid was opened in the nick of time, and so the contents of the bowel were able to escape by the tube, and gradually the over-stretched bowel came back to its natural state.

Next, what are the symptoms of chronic, increasing obstruction, and to what trouble may obstruction be due besides to cancer? Obstruction of the large intestine which is not due to cancer is comparatively rare. We will put aside such conditions as the mere obstruction by a lump of fæcal material, for that by itself—the so-called impaction of fæces without narrowing of the bowel—hardly ever causes complete obstruction. In a certain number of cases matting and adhesions cause obstruction, and this is more common in the female pelvis than in the male, because in the female pelvis there are more possible causes for inflammation and adhesions and scars. A woman was admitted into hospital because she was thought to have cancer of the rectum, and was sent to me in order that I might perform colotomy. I opened her abdomen so as to do colotomy, but before I opened the intestine I examined her pelvis and found the large intestine was bound down by adhesions, and these adhesions, as it turned out, were due to tubercular disease of her ovary and left tube. We divided the adhesions, and removed the diseased ovary and tube and freed the bowel, with the result that she did not have colotomy done, and is now quite well without it.

In another case I saw an old gentleman who was suffering from intestinal obstruction. His history was one of very long standing obstruction gradually increasing and finally becoming complete. So that when I saw him his abdomen measured nearly sixty inches in circumference, so great was the distension of the bowel. I opened the abdomen on the left side to do a colotomy, and so near was he to bursting that as soon as the support of the abdominal wall was removed from the immensely distended sigmoid flexure the bowel burst, though fortunately practically in my hand. We emptied it as quickly as possible and saved the peritoneal cavity from contamination, and then we found that he had bands of adhesion which had tied down his sigmoid. These bands were not due to cancer, but apparently to old dysentery. In his case the division of those bands led to him getting perfectly well. So that is another example illustrating that cancer of the large intestine is not the only cause of chronic obstruction.

In another case I saw an elderly lady who had had several serious attacks of intermittent intestinal obstruction at intervals of some months, and all of them rather of the nature of obstruction of the large intestine, that is to say much more distension and difficulty in emptying the bowel than there was pain and sickness. And after one of these attacks was over I opened her abdomen so as to see what there was which was causing trouble, and we found she had had pelvic peritonitis in the past, for some reason which we could not ascertain, and she had had a band of adhesions formed which was attached and lay across, and pulled upon her sigmoid flexure. And the division of that band brought to an end her attacks of intestinal obstruction. So remember it is not everybody with mechanical obstruction of the large intestine who has necessarily got cancer of it. And in order to show the changes in the bowel which result from the obstruction, I will ask you to look at these specimens, which illustrate that in cases where there is long-standing obstruction there is that hypertrophy of the muscle of the bowel, which tries to overcome the difficulty, just as the heart may increase in size to overcome its difficulties, or the bladder may increase in size so as to overcome obstruction caused by stricture. And as in the case of other muscular organs—the heart or bladder—so in the bowel, in addition to there being thickening and strengthening of muscular coats, there is liable also to be dilatation and distension of the cavity. The part which feels the distension most and shows most evidence of it is the cæcum. All the back-pressure from the distended bowel exerts its influence on the cæcum, and on the other hand it is into the cæcum that the small intestine continues to pass its contents, although the cæcum is already overfull.

Next, I want you to realise that in a certain number of cases of cancer of the bowel there is complete absence of that discharge of blood and mucus which is so characteristic of many others.

And I want you to appreciate that it will depend very much on the nature of the cancer whether there is this important symptom or whether there is not. And I also want to point out to you that, besides cancer of the bowel, there are other conditions which may themselves give rise to the discharge of blood and mucus. One of these is ulcerative colitis, another is dysentery, and another is tubercular disease of the intestine. All these may give rise to a discharge of mucus and blood, and you will see the conditions of ulcerative colitis in this specimen. In these cases there is, of course, the formation of pus and of mucus, and these ulcers bleed, and so people who have ulcerative colitis may have a discharge of blood and pus; and people with chronic dysentery, of which there is generally a definite history, may have a discharge of blood, pus, and mucus. Therefore, this discharge is not limited to cancer of the intestine, and there are also cases of cancer which do not have any of it, and for that reason they are more liable to be overlooked. Here are a series of specimens illustrating "annular" stricture of the sigmoid flexure, and it is in this condition, where the cancerous mass is very small and very fibrous, like "atrophic scirrhosis" of the breast, that the discharge of blood and mucus is very often practically absent, or, at any rate, it is unnoticed, so little of it is there. In these cases there is so little ulcerated surface and so little growth that there is very little mucus discharged, and there is very little bleeding. And what there is, especially when the growth is well up in the colon, is very liable to be lost sight of, being mixed with the fæcal contents of the bowel. Consequently the people who have these annular strictures are liable to have only troubles due to the narrowing of the lumen, such as much irregularity of the bowels, some colicky pains, a good deal of difficulty with flatulence, and some signs of what is commonly called by them "indigestion." And, beyond such troubles as that and constipation, nothing is obvious to indicate that there is cancer at all. But if these conditions go on, if a patient has frequent attacks of pain that is colicky, and flatulent distension of the bowel with inability to pass wind, all these things, you must remember, are compatible with the presence of a small cancer of this type in some part of the colon, and it is when it is in its early stage that you must recognise it and be prepared to advise, if necessary, an exploratory operation to see what is wrong. It is premature to say more at present about what I have to speak of with regard to treatment, but I will only mention that it is in these cases and in this stage that operation for removal of the cancerous growth is most successful. The people who have this condition of annular stricture of some part of the colon may have merely the intestinal troubles, such as I have mentioned, and that without any passage of mucus or blood. But yet any one of them, who perhaps has paid no particular attention to his symptoms, may at any time have the narrowed lumen of the bowel blocked up by a piece of fæcal matter, and he may have at once complete obstruction. A few years ago I saw a gentleman who had been seized with acute intestinal obstruction at a time when he was away from England. He was operated upon, and the intention of the operator was to do colotomy, but he missed the colon and opened a piece of small intestine. I think that really saved the patient's life. Afterwards it turned out that the patient had been liable to what he called "indigestion," and he had had frequent flatulent distension and bother with his bowels, for which, however, he did not consult his doctor. But when I subsequently opened his abdomen to see what there was we found he had an annular cancerous stricture of the intestine. It was quite capable of being excised, and, although he was æt. 75 years, he was strong, and at the present time, which is four years since the operation, he is alive and well. In other cases of cancer of the intestine, where there is a large growth and a fungating, protruding tumour, which grows into the cavity of the bowel, the discharge of blood and mucus is easily enough explained. The specimens which illustrate this best are too large to bring here, but they are in the museum, and you can see them for yourselves. This one specimen illustrates sufficiently well the conditions I am speaking of, where there is a cauliflower-like growth, which grows into the cavity of the bowel and bleeds and discharges very much mucus, and it is this discharge which attracts attention. But unfortunately the cases where there is much growth are generally not nearly so amenable to treatment as the others. Still, they are easier to diagnose. The cases of annular stricture are very often missed because there is not the characteristic discharge.

Now a word about cancers of the rectum itself. On examining the man who is now in Darker Ward we found that he has cancer high up in his rectum. He has now no bad pain, and in the early days he had no pain at all. You will remember that when I was speaking last week about cancer of the breast I said it was unfortunate that the public did not realise that cancer in its early stages is painless. When cancer occurs in the rectum it is often, in its early and removable stages, painless. In proportion as it is near to the anus it gives rise to abnormal sensations or to real pain. The nearer it begins to the anus the sooner will the anus be infected by invasion, and the earlier it is affected the earlier the patient appreciates the presence of something abnormal and seeks advice. When the cancer is three or four, or five or six inches up it is liable to cause no pain whatever, and in many cases it is of considerable size before the patient has any idea that there is anything serious the matter with him at all.

We lastly come to the question of the treatment of complete obstruction in these cases. Suppose that a patient, of whom you know nothing, has difficulty in getting his bowels opened and sends for you, telling you that there has been trouble for three or four days or more, and that he has taken medicine which has had no effect. What advice will you give such a man? Of course you are not going to jump to the conclusion that he has intestinal obstruction and requires operation, and what you will advise depends on what he has had in the way of medicine. Supposing for the moment that a dose of castor oil has been taken, or that other aperients have been given, perhaps in increasing quantities, what is the next thing to do? Certainly avoid giving any more purgatives, and avoid them all the more if the patient cannot pass wind. There is no question about this; mere difficulty in getting the bowels to be satisfactorily emptied is a matter of totally different significance to being unable to pass flatus. And if your patient is unable to pass any flatus you must not give any kind of aperient whatever. There is a great tendency, when a patient's bowels are obstinate, to keep on pouring medicine into them to get them to act. If you do that when there is complete obstruction of a mechanical character and there is no passage for the contents of the bowel, you will bring about, in the course of twenty-four or thirty-six hours, a condition of dangerous distension, which would, if you had not given that medicine, have taken at least a week or two to bring about. If a patient has obstruction which will not let anything pass and you give him purgatives which cause a large watery flow into the intestine, you will distend the intestine in thirty-six hours more dangerously than it would distend itself in a week. So not only is such treatment harmful but it is extremely dangerous, and if you have the least suspicion that a person does not pass wind do not give any aperient at all. The only thing you are justified in giving is an enema. Enemas of soap and water, or turpentine, or assafœtida, or castor-oil, or olive oil, may be used. These do not do any actual harm even if they do not do good, and by using them you are not doing anything which will increase the amount of material in the intestine above the obstruction.

The next conditions we come to are those where these methods of treatment are useless. The only alternative, of course, is to relieve the obstruction by operation, so we will suppose you have opened the abdomen. You may find a distended sigmoid flexure, and below that a lump of cancer, which could easily be removed. What will you do? Well, never try to remove that cancer at this time. If you undertake the operation of excision of this cancerous growth which causes obstruction at a moment when the bowel is enormously distended, you are almost certain to lose the patient's life. Some few years ago a gentleman was sent up to London with intestinal obstruction of several days' duration. He had an enormously distended abdomen, and there was a history of two attacks of obstruction within the last six or nine months, though he had no history of any discharge of mucus or blood. We considered it probable that he had cancer, or that possibly he might have obstruction of the large intestine due to something else. It was evident that he must have colotomy done at once, because he was so distended that it was useless to wait. So I opened his abdomen and then his sigmoid flexure, which was very large. When we had a tube safely tied into that and it was possible to examine his abdomen, I could find about three inches below where I had opened this distended bowel that there was a lump of very hard cancer, and an annular stricture of his colon at the sigmoid flexure. For five days we drained

the bowel through the tube, and on the sixth day we opened up the wound and drew out this nodule of cancer and excised it. We closed the colotomy aperture as well and joined the severed colon, and four years afterwards the patient is perfectly well. Do not think he would have been alive at all if I had set to work to excise his cancer and sew up the ends of the intestine when the bowel was enormously distended, because no suturing would have held under those circumstances. So, if you do a colotomy for obstruction and you find cancerous growth do not be tempted to excise it at the time. I mentioned to you that in the cases where there is annular stricture, in many of them the patient has only the history of flatulent distension of the abdomen, colicky pains, and perhaps slight attacks of more or less complete obstruction. Well, if you think that such a patient has possibly a growth in the bowel then is the time to open the abdomen, before the other and worse symptoms of obstruction come on. I saw a lady, æt. 51 years, who had had attacks of this kind, and who, fortunately for herself, developed a small lump, which could be felt *per vaginam* and was very movable. It was thought by those who saw her to be a diseased and enlarged ovary, but when I came to examine it myself it did not feel like an enlarged ovary, and with this history of colicky pains and flatulent distension of the bowel from time to time I said it was quite likely that this lump might turn out to be a lump of cancer; one argument against it being so was that it was so movable. But cancer of the sigmoid flexure is movable at first, for there is a time before which it contracts adhesions to anything. We opened her abdomen, therefore, and found a cancerous annular stricture of her intestine; we cut away the affected piece of bowel, sutured it up, and now, nine years afterwards, she remains perfectly well. So if you get these cases sufficiently early, if you do not wait until the signs are so obtrusive that your diagnosis of cancer can be made positive by reason of the extent to which the disease has been allowed to grow, the prognosis of these cases of annular stricture and small growths is exceedingly good after recovery from operation.

I mentioned to you just now that in the case of this patient who is in Darker Ward we found that he had a cancerous growth of his rectum three or four inches up. And the question arises, after having relieved this patient of the intestinal obstruction, and his abdomen is no longer distended but empty, What about removing this growth? That is one of the things which has always got to be balanced in connection with the condition of the patient and the evidence of more extensive disease. As far as this man is concerned, I am afraid there is no reasonable probability that he will be well enough and strong enough to undergo such an operation as will be necessary to excise his rectum. Excision of the rectum is an operation which, when undertaken for small growths or growths quite low down, may be done without any very great risk to life, but in proportion as the growth is high up, and perhaps a considerable portion of the coccyx and sacrum have to be removed also, the operation becomes more extensive, and becomes naturally associated with a good deal of shock. And old and feeble people who are run down through illness and have had their nourishment much impaired are not able to stand it, and a large proportion of such people die if the operation is attempted. So you have to try and hold the balance evenly, and estimate whether any particular patient is likely to stand removal of the rectum. I do not think our patient is strong enough to go through such an operation as that, but we will see what progress he makes in general health. You must remember he has recently had intestinal obstruction, that he has consequently been unable to take his food, and that he is ill. He may of course get strong enough to stand the operation, or at all events to encourage one to try it. But I will tell you of a case I saw a few months ago, in which an old gentleman had had colotomy done, and afterwards I was asked to see him with the view of excising his rectum for a growth. It was an accessible growth, and it could have been removed by taking away the lower four or five inches of bowel. But he was very feeble, he had a weak and irregular heart, and he had had several fainting fits. I therefore came to the conclusion that the operation was more than he could stand, and that if it were attempted it would kill him. Therefore we decided not to do it, and advised the patient to put up with the colotomy wound and not to have anything further attempted. Within six weeks of my seeing him he had an attack of cardiac syncope, from which he died, and there can be no reasonable doubt that if we had done an operation he would have died during the operation or immediately after it. So you have to

adapt your treatment in regard to the removal of these growths to the condition of the patient and his ability to bear a large operation. Excision of the rectum is a much more trying operation for the patient to go through, and is associated with more shock than is the removal of a cancerous piece of the colon inside the peritoneum, when it is not adherent to other structures. So that in cancer of the intestine, although you might be inclined to think that a cancer inside the abdomen was worse to deal with than cancer of the rectum, I think as a matter of fact it is not so, and if you make your diagnosis before the growth has existed too long you will be able to save many lives.

July 19th, 1909.

Prophylactic Treatment of Eclampsia.—Stroganoff states that his method of prophylaxis of eclampsia has been applied in 360 cases at St. Petersburg, and the mortality of this disease has been reduced to 6·6 per cent. for the mothers and to 21·6 per cent. for the children. He reiterates that he knows of no disease in which therapeutic measures display more brilliant results than in eclampsia, and he urges the more general adoption of his technique. It aims to prevent the convulsions by reducing the irritability of the nervous system, obtaining tranquil sleep by means of narcotics, and removing everything liable to induce irritation, terminating the pregnancy if necessary, and watching over the regular action of heart, lungs, and kidneys, placing the patient in the most favourable positions, administering oxygen in abundance, and keeping the patient under the influence of morphin and chloral, with chloroform at first until the patient feels the effect of the chloral. In moderately severe cases, first morphin, about 0·015 grm.; in one hour or sooner, 2 grm. chloral; morphin again the third hour; chloral the seventh; and 1·5 grm. chloral again the thirteenth and twenty-first hour. Delivery is hastened as necessary, and fluids are supplied by the rectum or mouth, from 150 to 250 c.c. four or five times a day. The aim is to prevent the convulsions, even if as much as 4 or 5 grm. chloral and 0·03 or ·04 grm. morphin plus chloroform occasionally are required in the course of five or six hours. If the convulsions keep up obstinately delivery is hastened. Vaginal Cæsarean section is indicated if necessary. —*Journ. A. M. A.*, vol. liii, No. 1.

A LECTURE

ON

MITRAL STENOSIS IN CHILDHOOD.

Delivered at the Hospital for Sick Children.

By F. J. POYNTON, M.D., F.R.C.P.Lond.,
Physician to Out-patients, the Hospital for Sick Children, Great Ormond Street; Assistant Physician to University College Hospital.

In the study of heart disease there are few more interesting subjects than that of mitral stenosis, for the condition is one of much frequency and of great gravity, and the origin and development of the condition leads us to pathological problems which are exceedingly difficult to solve. I shall not attempt in this lecture a clinical description of mitral stenosis, for that has been done many times, and by some of the great masters of medicine, but I shall be content to dwell upon some of the points which are not quite so commonly dealt with. No one, I think, can really understand mitral stenosis unless they have had experience of heart disease in the young, for as a rule in adults we see the malady either fully developed or complicated by the terminal events which result from failure of compensation. If content to study it only in the adult, we are also in danger of finding ourselves accepting a mysterious origin for the disease or falling back upon its congenital development more often than is justified.

A congenital mitral stenosis cannot be denied, but I feel sure it is an exceedingly rare event, for in ten years' experience here I can only recall one, or possibly two cases, which I date with any confidence from birth.

As to the cause of this condition I am convinced that rheumatism is the outstanding one, and that form in particular which is associated with repeated attacks of chorea. Here, for a moment, I must digress, in order to add that I hold that the vast majority of cases of chorea in this country are rheumatic. I will not say all, because it appears to me unscientific to make such a statement in face of the observations of others to the contrary, and also because we are not able to explain the exact processes by which chorea is produced. How, then,

I would ask, since we lack such exact knowledge can we dogmatically assert that only one morbid process can produce chorea?

I interpolate these remarks because in cases of mitral stenosis in adult life you may get no history of "rheumatism in joints" but you may get one of chorea, and that means almost certainly rheumatism. The absence of any history of arthritis does not necessarily mean that the origin of the stenosis is mysterious. I have many times now traced the development of mitral stenosis in children who have suffered from repeated chorea, and have watched some of them later at University College Hospital, after they have reached the age of twelve, until they have drifted into the condition which we all recognise as classical.

The next point I wish to dwell upon is concerned with the life-history of the rheumatic infection. It is almost generally accepted now that it is an infection which may at one time or another attack almost all the important organs of the body, and in childhood its manifestations are almost always multiple. There are, however, exceptions to this rule. Thus chorea may be the solitary manifestation, or arthritis, or, I believe, pleurisy, and sometimes, though very rarely, nodules. I need hardly add that cardiac disease may be the sole manifestation, or if not absolutely the solitary evidence, at any rate so nearly so that the other rheumatic symptoms have been overlooked, which for our purpose comes to the same thing. The point I wish to make is this, that among cases of mitral stenosis of mysterious origin we must allow a group in which the only rheumatic symptom to attract attention is this cardiac affection. This is not an attempt on my part to assume what is to be proved; it is a legitimate conclusion from our knowledge of the history of rheumatism, and is no more remarkable than the occurrence of a solitary tubercular lesion. Again, we must allow that cardiac rheumatism may be overlooked in early life. Rheumatism may have been present, but it did not alarm the parents, and sometimes medical men have been caught off their guard.

Aortic regurgitation and mitral stenosis have both in my experience escaped recognition in childhood. At the present moment I could put my hand on the case of a young woman who, I am glad to say, is in the Government employ, with very obvious cardiac disease. I had watched her for some years and seen her with active cardiac rheumatism, yet in spite of my assertion that she would never pass the doctor, she did so, to the advantage of herself and the Government. I mention these facts to show that we are none of us infallible, and to emphasise that all cases of mysterious heart disease are not necessarily so very extraordinary in their origin. Again, we must remember that cardiac rheumatism may begin at a very early age, and I must refer you to a paper in the 'Quarterly Journal of Medicine' for 1908 for some recent evidence in support of this fact, which must be taken into account before deciding that any left-sided valvular lesion is a congenital and not acquired one.

To sum up, then, if we tabulate laboriously all cases of mitral stenosis which give a history of rheumatism or chorea, or failing this, develop them later while under our observation, and if in addition we allow a small margin for error, and for pure primary cardiac rheumatism, it is surprising how the mysterious origin of mitral stenosis whittles itself down to scanty dimensions.

There are, nevertheless, cases of mitral stenosis of mysterious origin, and their frequency is just sufficient to rouse us the more to persevere in the study of the life-history and treatment of rheumatism.

There are, for example, the congenital cases, which for teaching purposes I divide into those complicated with other congenital lesions and those suggestive of intra-uterine endocarditis. It is not a scientific or even good classification, but is opportune because it helps to remind us of two interesting points in the study of congenital heart disease, namely the possibility of a true arrest of development, and, on the other hand, the occurrence of intra-uterine infections. I have never to my knowledge seen a case of congenital mitral stenosis with other congenital defects associated: such a case, of course, suggests that the heart affection is a true factor in development. Gilbert and Rathery, Heitz and Sezary have recorded some interesting facts on this point. Thus Heitz and Sezary record a case in a man, æt. 48 years, associated with hemihypertrophy of the left side of the body, and another case with marked infantilism of the Gilbert and Rathery type. Labadie, Lagrave, and Dupuy have described another in a girl with congenital hypertrophy of the breasts, Demoulard one in

a man associated with syndactily. Hare-lip and sternal malformations are also on record. You will allow that these are very suggestive examples, but unless the evidence of heart disease dates from birth, we must admit the possibility that the victim of a congenital malformation other than the heart might also acquire mitral stenosis. I would warn you against the assumption that a small frame and stunted development are proofs of the congenital origin of mitral stenosis, for that condition acquired in early life may cause serious arrest in development, as Heitz and Sezary thoroughly appreciated.

A few post-mortem examinations have been made upon cases of mitral stenosis associated with congenital malformations, and it is curious to note that both Faure's case, and Klippel and Clerc's two of this type, showed a condition of the mitral valve which pointed to an intra-uterine inflammation rather than a true arrest in development.

Intra-uterine endocarditis is a fascinating page in the history of heart disease, and there are remarkable clinical facts on record with regard to it, particularly, as you would expect, in association with rheumatism. Thus for example: A mother has been attacked by rheumatic fever in the late months of pregnancy, and the child *in utero* has developed a cardiac murmur, and has been born with heart disease. In my small book on heart disease I record a fact of my own observation. The child of a mother the victim of an attack of rheumatic fever in late pregnancy died on the second day after birth of congenital heart disease.* I found exuberant vegetations on the mitral valve forming a relative stenosis, and these vegetations contained numerous diplo-streptococci indistinguishable morphologically from the *Diplococcus rheumaticus*.

Dr. Theodore Fisher showed a post-mortem specimen of congenital mitral stenosis in 1902 at the Society for the Study of Disease in Children. In that case the mitral opening was not one tenth of an inch across although the child was fifteen months old. The chordæ tendineæ were thickened and shortened. Sansom, Cotton, and others have also recorded like examples.

I don't think it is difficult to understand a congenital mitral stenosis as a result of intra-uterine infection. All that is needed is a subacute infection at any early date. It will require but a very slight degree of inflammation to glue together the minute cusps of a fœtal mitral valve. Nevertheless, the event is one of extreme rarity.

This boy is one of the most likely examples of this class of case that I have come across.

He was brought to me in April, 1906, for heart disease. There was a marked history of rheumatism in the mother's family. His maternal grandmother and his uncle had both suffered severely from rheumatic fever. He was a premature child, and at his birth the doctor detected heart disease.

He came to me at the age of two years, never having had any rheumatism though he had suffered from bronchitis and pneumonia, and I found mitral stenosis and regurgitation, stenosis being the chief feature. This case is not above suspicion, but it comes very near to the necessary tests for the diagnosis of congenital mitral stenosis.

Can other infections produce mitral stenosis besides the rheumatic? The answer is, I believe, much the same as that which I have already given in my remarks on chorea. Other infections may do so, but probably very rarely.

The first condition that comes to mind is mitral stenosis following scarlet fever. In my opinion this is rheumatic, and later in the year I am bringing some more evidence forward to support this view, which Sir Thomas Barlow many years ago believed to be the explanation of at least *some* cases of scarlatinal rheumatism.

Again tuberculosis may, I am sure, though rarely, produce mitral stenosis by a process of calcification of the mitral segments. Other cases follow diphtheria and measles, but of these I will say no more than that in both these diseases there occurs sore throat, and here again we may be dealing with the rheumatic infection.

I come next to the very practical question of the various ways in which acquired mitral stenosis appears in childhood. Naturally I put aside all cases which have come here with the conditions declared; for these the interpretation of the earliest phases must be one of surmise.

The first case I mention and show is a rare one. In March, 1902, a girl, æt. 9 years, who lived in a damp house, was brought here for severe chorea and with it remarkable tachycardia. She was exceedingly nervous, but there were no signs of Graves' disease. She remained in the hospital for two months with a pulse-rate varying from 140 to 200 beats per minute. The only murmur ever

detected was a faint systolic apical bruit, which disappeared and was only occasionally present. In the following July she came to me again for tachycardia, but there was no bruit. Since then I have followed her for seven years through two more attacks of chorea, and she has now well-marked mitral stenosis with the characteristic thrill and loud rumbling murmur.

All these years tachycardia has appeared from time to time, and the child has been highly excitable. The great interest in this case has been the early appearance of tachycardia—a symptom which we recognise in the advanced stenosis of adults as one of the most troublesome dangers of the disease. Here it appeared before the stenosis and has remained prominent. Since that date I have seen a few similar cases, and they always suggest to me a neuro-muscular rheumatic affection of the heart, which seems the more likely when we remember how closely associated are muscular rheumatism and rheumatic neuritis in connection with the skeletal muscles.

The occurrence of persistent tachycardia in children suffering from cardiac rheumatism must thus make us on guard for mitral stenosis.

I will next take an example of the appearance of mitral stenosis in early childhood arising in connection with repeated attacks of chorea. I am indebted to Dr. Voelcker for allowing me to show this patient, who is at present under his care in the Clarence Ward.

This child here came to see me first in January, 1903, with the history of a severe cold and sore throat lasting seven days. On the fourth day of the illness chorea commenced, and when I saw her there was in addition a dilated heart with a well-marked mitral regurgitant bruit. She recovered in the hospital, but two months later I made a note that the first sound was becoming abrupt and foretold the supervention of mitral stenosis. Since 1903 this child, who was then only $2\frac{9}{12}$ years old, has hardly ever been absolutely free of chorea, and is now just passing through a seventh attack. In 1907 I noted well-marked stenosis, and that is, of course, present to-day.

This is a good example of the usual way in which mitral stenosis appears: first there is a dilated heart with a mitral regurgitant bruit; then later, with repeated rheumatism, stenosis begins, and though the lesion is a double mitral, one finds as years go by that the contraction of the orifice gains the upper hand.

Let me warn you that during this process of contraction there may be a period when the mitral regurgitant bruit disappears, and then if you overlook the abrupt first sound you may think the heart has recovered and is sound.

When you bear in mind that this child's first attack of rheumatism was at $2\frac{9}{12}$ years you can easily understand that it would be tempting to fall back on a congenital origin for the mitral stenosis.

In my paper on rheumatism at and under five years of age I record another parallel case beginning with chorea at an even earlier age. This case was also relapsing in type and associated with mitral stenosis.

A third way in which mitral stenosis may appear is exemplified by the following case: In December, 1902, M. J—, æt. 9 years, came here for a second attack of chorea of the usual type. On examination of the heart I found no murmur, but the well-known triple apical sound represented by the sounds tut-tŭt-tŭt. These sounds persisted, and I noted then the probability that there was some stiffening of the mitral segments. Since that date I have seen this child from time to time, and she is now a girl of sixteen with extreme mitral stenosis. There is a loud, rumbling, presystolic murmur, leading up to a short, sharp first sound, but there has never been an obvious systolic murmur.

Another attack of chorea occurred three years ago, and about twice a year she comes with a few fleeting muscular pains, but there has never been an attack of rheumatic arthritis, although during the last year she has developed breathlessness and palpitation—sure signs that her heart is already beginning to reach the limit of compensation.

In this case, from the first a presystolic murmur and the early development of a thrill were the cardinal features. Chorea was never severe, and other evidences of rheumatism were very insignificant. This is a history which, in my experience, we are liable to get in cases in which the signs of mitral stenosis are prominent from the first, and these are also the cases in which a history of rheumatism is very likely to be denied.

When you consider the great gravity of mitral stenosis in adult life, and recall the numerous

cases you have seen in general hospitals, it must strike you how insidiously the early stages are developed in childhood. If, on the other hand, you devoted all your attention to children, you might be led to think these minutiæ of clinical observation are of but little real importance, because it is certainly rare under twelve years to find an advanced mitral stenosis. You see the early stage in childhood; you learn the gravity of the lesion in the adult. Mitral stenosis is more common in females than in males, as is also its frequent concomitant, chorea, and the explanation for this always seems to me to be one of the most subtle of pathological problems. I cannot help feeling that it is greatly dependent upon some difference in the vital reaction of the female tissues to the rheumatic poisons. There must be, I believe, a very real difference in many of the biochemical reactions of male and female, and hidden somewhere in these lies the fact that rheumatism in the female is often more smouldering than in the male. The so-called rheumatoid affections of joints are more frequent in the female, and it seems not unlikely that in mitral stenosis you have a cardiac lesion akin to the relapsing subacute contracting form of rheumatoid arthritis. Both may appear in the male, but they are both more frequent in the female.

I want now to spend a short time in contrasting mitral stenosis in its most classical form with another type of rheumatic heart disease met with in children, which for the moment I shall term the "gaping mitral." Mitral regurgitation due to valvular disease is, no doubt, generally the least harmful of all lesions. A slight mitral leak may exist for many years with no deviation from good health, and if the patient is not one of those unfortunately nervous people who is always alarmed by the fear of organic heart disease, it may even prove a safeguard by reminding him that a certain prudence in life is advisable. In spite of this general truth, it is also well known that certain cases of mitral regurgitation in children are of the worst prognosis. They are in my experience more frequent in males, and are the result of a virulent type of cardiac rheumatism. I do not mean by this the malignant type of rheumatic endocarditis, which I hold is most frequent in adolescence, but a malignant form of rheumatism which greatly damages the myocardium, and incidentally, as it were, damages the mitral valve. Post-mortem examination always shows the same result: a large dilated heart, with or without pericarditic adhesion, pale muscle, showing changes which I demonstrated ten years ago, but which have been most carefully and more completely worked out by Dr. Coombs, in 1908, and lastly a gaping mitral opening with valve segments obviously but not grossly diseased.

These cases form a great contrast to cases of mitral stenosis. In both there are recurrent attacks of rheumatism, but in these virulent cases the rheumatism is much more severe. There is profound anæmia, and there may be nodules, and for long periods, such as eighteen months, there may be no real cessation of rheumatism.

Breathlessness and tachycardia appear early and the well-known to-and-fro mitral bruit may soon make its appearance.

In these cases, however, it is not the mitral regurgitation that is the destructive process, though it may be very considerable, but it is the persistent malignant rheumatic carditis that is ruining the cardiac muscle, and preventing any satisfactory attempt to cope with the coincident mitral lesion.

We cannot judge such cases from the fact that there is a mitral systolic murmur—that is to take a most imperfect view of the condition. It is the type of rheumatism that must arrest your attention, and I believe it to be a type more frequent in males than females.

The interpretation of these conditions of stenosis and regurgitation is to me much easier if we put aside that difficult term "rheumatic fever." Let me put to you that we use for tubercular disease a general term, "tuberculosis," and let me ask you to use in a like sense the term "rheumatism." When we meet with a case of tuberculosis we see it often enough run a prolonged course with exacerbations, and I am not sure that we should care to bind ourselves as to whether these exacerbations are the result of fresh infection or the flaring up of quiescent foci improperly healed. I would ask you to apply the same line of thought to rheumatism, and you soon find yourselves convinced that what we may have considered to be an attack of rheumatism which has run its course, as measured by temporary improvement, is in reality an attack which has by no means run its course, any more than a case of tuberculosis which

has made temporary improvement has necessarily run its course. The disease is there, and in the virulent cases bursts out again at intervals, and, indeed, may never really be quite quiescent. There may be fresh infection, but I am quite sure that is often only a flare-up of the primary one. Let me once more compare tuberculosis: We all know the cases that give trouble from time to time but run a slow course with abundant fibrosis of tissue, and those, too, which break out with hectic fever, softening and excavation. Early in the course of these latter you recognise that though life may be prolonged for some while the patient is doomed, for the type is virulent. I hold that we may recognise in cardiac rheumatism similar events.

The lesson we learn of course is this: in judging of a case of rheumatic heart disease in childhood, we must not be content to collect the physical signs and judge by these alone; we must also try to estimate the type of rheumatism, and also the constitution of the child. There is a very great deal of difference in the resistance of children to rheumatism, and some of the most graceful and brightest are particularly liable to go downhill rapidly.

The diagnosis of mitral stenosis is not by any means always an easy matter. The cases which are the most readily recognised are the group in which the *crescendo*, rumbling, presystolic murmur is prominent early in the illness. In such the presystolic thrill may be most marked, and the accentuated and reduplicated pulmonary second sound aids in the decision. You know the congested face and the curiously translucent appearance of the eyes; sometimes there is marked arrest in development and very obvious clubbing of the fingers. In the very extreme cases embolisms and even gangrene of the extremities may occur, and the child may literally die by inches. In other cases repeated bronchitis and hæmoptysis occur as in adults.

Difficulties, however, arise in diagnosis when there is no murmur, and only an abrupt first sound, tachycardia, and breathlessness. In such cases you may feel doubtful for some while as to the exact condition.

Again, the murmurs audible over the impulse in the diastolic phase of the heart may often be confusing. The rumbling presystolic murmur is easy, but the softer diastolic murmurs by no means always mean stenosis, although they may be mitral in origin. An adherent pericardium with mitral regurgitation and cardiac dilatation will give a to-and-fro murmur, the diastolic element of which does not signify mitral stenosis. It is, I think, possible to become almost too academic in the attempt to diagnose mitral stenosis. Often enough there may be a little thickening of the ring of the valve which does not produce a practical stenosis, and we may worry ourselves over this detail and lose signs of the real importance of the case as one of heart disease. On the other hand, when there is continued slight rheumatism or repeated chorea we cannot be too much on guard for the abrupt first sound, the presystolic thrill and murmur, the small pulse and accentuated pulmonary second, which are the most important warnings of mitral stenosis.

Mitral stenosis is rarely fatal in childhood; the lesion itself does not reach such an advanced stage before the twelfth year. A child may die from acute rheumatism complicating a coincident stenosis, but death from failure of compensation is rare. The lesion is quite incurable, but there is a great difference in the rate of progress. No doubt some cases arrest, and we know that women have had large families and lived to old age suffering from mitral stenosis. If the disease makes rapid progress in childhood and adolescence life will not be long, and there will probably be some years of repeated cardiac breakdowns and much ill-health before the fatal illness. We want, I think, more clinical observation upon the progress of stenosis in adult life. Such experience as I have had leads me to be very suspicious of cases of mitral stenosis which from time to time suffer from arthritis or rheumatic pains. It is difficult not to think that this must mean a smouldering activity in the rheumatic process and consequent advance in the contraction.

If you have the care of children with mitral stenosis or its warnings you will doubtless have to deal, later, with the question of marriage, but fortunately you will probably not have to settle it; you may advise, but have no power to insist. For my own part I am at variance with many who hold that marriage should not be entertained, for many have lived happily and had families. The dangers should certainly be pointed out and their imminence in the particular case carefully considered. Yet even suppose against advice

marriage is entered upon, and the mother dies early in life as a result, and leaves a child who becomes a genius, can we short-sighted medical men decide which of the two decisions was the wiser? And even if children are left motherless, can we deny the possibility that these motherless children may not find protectors and lead happy and useful lives to the comfort of others?

The treatment of mitral stenosis in childhood is mainly the treatment of rheumatism. Warn the parents of the meaning of sore throats, fleeting pains, nervousness and chorea, feverishness and pallor. If possible get such children taken from damp, low-lying houses, and see that they are properly clothed and their extremities protected. Large unhealthy tonsils should be enucleated as Mr. G. Waugh advises. Spring and autumn, and particularly sudden damp cold after much heat, should be a signal for added watchfulness. Early symptoms should be promptly treated by rest and warmth, and the use of salicylate of soda. If you were a strict believer in the specific action of salicylate of sodium I think you would give these children long courses, interrupted at intervals. As yet I have not had sufficent faith in the specific action to attempt this long and necessarily expensive treatment on such a scale, but I should be exceedingly interested to read the report of such an experience extending over many years and embracing many cases, and undertaken by an unbiassed observer. Such an undertaking would be a formidable one, but it might settle the vexed question of the exact value of salicylate of sodium in rheumatism, and perhaps achieve a result far greater than one expects. Should this prove to be the case then Dr. Lees, who has striven so much while at this hospital for the cause of the rheumatic child, would earn our everlasting gratitude.

July 19th, 1909.

We have received from Messrs. Shaw and Sons, of Fetter Lane, London, a copy of 'Symptoms and their Interpretation,' by James Mackenzie, M.D., F.R.C.P. The author, in his preface, says that the early stages of disease are not fully appreciated, and can never be so till the general practitioner takes his position as an investigator. This is very true, and when the general practitioner does this work a great step forward will be made towards the elucidation of the nature of early symptoms and prognosis of disease.

ON THE TREATMENT OF NEURASTHENIA AND THE RELATION OF THIS DISEASE TO EXOPHTHALMIC GOITRE.

A Lecture delivered at the Polyclinic, Chenies Street, London, W.C.

By THOMAS D. SAVILL, M.D.Lond.,

Physician to the West-End Hospital for Diseases of the Nervous System and to the St. John's Hospital for Skin Diseases.

Gentlemen,—The topic of my discourse to-day is the treatment of neurasthenia. Incidentally I also want to offer you some remarks on the relationship which neurasthenia bears to exophthalmic goitre or Graves' disease.

You are no doubt acquainted with the meaning of the term "neurasthenia"—that it means nervous prostration, an irritable weakness of the entire nervous system, the brain, spinal cord, and sympathetic system. There are some who regard it always as of mental or cerebral origin, but it is always the entire nervous system which is involved, though one part may be more affected than another. It is not the same disease as hysteria; it differs from that in its age-incidence. Young middle life is the favourite age, but neurasthenia may come at any age. In hysteria the first manifestation nearly always is at or about puberty, or between that and twenty-five; always under thirty. There is also a different sex-incidence in the two diseases. Ninety-five per cent. of the subjects of hysteria are females, whereas in neurasthenia young adult males slightly preponderate.

In former times neurasthenia was regarded as a very unenviable condition. In order that we may profitably consider the question of treatment it is necessary that we should first consider the ætiology, for it is only by the *recognition and treatment of the cause* that we can really eradicate the disease. Now the conclusion at which I have arrived is that the causes are most varied, and consequently the treatment is widely different in different cases. It is only by prolonged investigation into the cause or causes in operation in any particular case that a satisfactory scheme of treatment can be adopted. There are four groups of causes. The first of these is fatigue or overwork, and that you are no doubt quite familiar with in every-day practice. Just as a faradic battery will become weaker and weaker if

it is used and will be restored by rest and warmth, so will the nervous system become weaker and weaker if it is overworked, that is, if there is prolonged forced functioning. And one meets with many different conditions which produce it in that group. The second group is that of malnutrition, where for some reason the body, or the nervous system, is impoverished by insufficient nourishment or by previous disease. Post-influenzal neurasthenia probably belongs to the malnutrition group. The third group is that of shock, which may be of two different kinds, though really the same clinically. There may be grief, or worry, or anxiety, all of which come under the heading "emotional shock," or there may be nervous shock from surgical operations, which may be followed by neurasthenia, or from accidents. These are three groups universally admitted to be general causes of neurasthenia. Up to the year 1896 they were, as far as I know, the only causes which were seriously regarded as legitimate causes of neurasthenia. And the treatment advocated consisted of rest, nerve tonics, feeding, fresh air, and change of scene.

In the years 1896–7, after studying the disease for a considerable time I came to the conclusion that there was in a great many cases a toxæmia in operation, and I arrived at that conclusion in this way. First of all I found, by an investigation into my hospital cases, among the out-patients, that the dyspepsia, or rather the gastric symptoms which were so frequently associated with the disease, and which had by many observers, even by Charcot, been regarded as part of the disease, very often came on before the neurasthenia—in other words, the gastric symptoms antedated the nerve symptoms. Therefore I made further inquiry, and found that the gastric troubles had been complained of for months or years before any nerve disorder appeared in more than half if my memory serves me. Secondly, I found that by attention to the gastric disorder one could cure the neurasthenic symptoms. Therefore I concluded that the gastric disorder was really the cause, not the consequence, as many authorities had previously thought. They spoke of "gastric neurasthenia," "neurasthenic gastroptosis," and various other terms, as indicating that those disorders were consequences or symptoms of the neurasthenia.

Next, by a series of arguments and investigations I concluded that gastric disorder produced neurasthenia by means of a toxæmia.* Thirdly, I found that there were other toxæmias which could come into play in the production of neurasthenia. Those data I have put forth in various publications. I need hardly tell you that the treatment for fatigue, malnutrition, and emotional shock really consists of well-directed feeding, psychic treatment, rest, nerve tonics, and sometimes Weir-Mitchell treatment. But these did not always answer. That was one reason which made me turn my attention to the possibility of other causes. Fatigue, malnutrition, and emotional shock are admittedly in operation in some cases; in a series of 103 private cases which I investigated these three causes came into operation in 4 per cent., 7 per cent., and 2 per cent. respectively. It is very likely that in hospital cases those proportions would be altered. When the treatment was directed only to those conditions the disease had often been regarded as incurable. The remedies I have mentioned—rest, psychic treatment, nerve tonics, nutrition, and Weir-Mitchell treatment—failed, and the cases were regarded as intractable until I directed attention to various other causes of toxæmia.

Among the toxæmias which may be in operation are these I have placed on the blackboard, and I have put down the proportion among 103 private cases. Thirty-one per cent. were preceded by gastric disorders of various kinds, particularly gastric dilatation, gastric myasthenia, that is to say, weakness of the stomach wall and retention of its contents. Intestinal disorders formed about 39 per cent. So the gastro-intestinal conditions account for nearly 70 per cent. of the toxæmias. Pyorrhæa, oral sepsis, and other septic conditions account for about 12 per cent., and incipient tuberculosis and other infective conditions about 8 per cent. And "sundries," consisting of various complex causes, where it was impossible to identify the real individual cause which was in operation, account for the remainder. One of the difficulties of this subject consists in the fact that there are nearly always two or more causes in operation. There is in many cases a predisposition on the part of the individual to nerve weakness; and when that individual gets one of these conditions he goes downhill. There are other complex con-

* 'Lectures on Neurasthenia,' fourth edition, Glaisher and Co., London, 1908.

tributory causes, like high tension, cardio-valvular disease, and renal disease. One patient had renal disease, over-work, and various other things, and one could not attribute the condition to a single cause.

In regard to toxæmia of course one has to identify what particular toxæmia is chiefly in operation, and that is a difficult matter. There are two practical hints which I can give you, in the first place as to the means of identifying toxæmia. The first is this: that when you get a toxæmia in a patient you very often find a dusky and mottled appearance of the skin, which is very characteristic when you have once identified it. It is a condition which I pointed out in my lecture on vaso-motor conditions,* a mottling which is like a faint indication of the old eruption of typhus, which, perhaps, many of you have not seen. It is a very fine mottling indeed, and one has to take a bird's-eye view of the skin to see it. With that is often associated a blear-eyed look in the patient; the eyes are not clear. This is particularly so in the case of intestinal toxæmias, such as colitis, and incipient intestinal sepsis of various kinds. The second hint is, that in searching for a toxæmia it is very useful to make your search from above downwards, *i.e.* to make search in or about all the mucous passages in the following order: Inquire about the nose or throat, whether there is anything in the antrum, the teeth, or the gums. Among hospital patients, for instance, pyorrhœa alveolaris is one of the most frequent septic conditions in operation. But in my list of private patients it comes quite low down; I think there were only about 5 cases of pyorrhœa in these 103 cases.

Among hospital patients who come with neurasthenic symptoms one finds the gums in a spongy ulcerating condition. Then, again, there may be ulceration or derangement of the stomach, or of the intestinal canal, the uterus, the vagina, the bladder. In or about any of these places is where one searches for evidences of a toxic condition, and very often it is difficult to identify them. It is particularly difficult in certain cases where there are intestinal conditions, where the patient cannot help you in the slightest degree. They have never observed their stools, and they may say very casually, "Yes, I am very constipated." Or they say, "No, the bowels act regularly." "How often?" "Every other day sometimes." "Do they act once a week?" "Yes, mostly." Another patient will tell you that he or she has alternating periods of diarrhœa and constipation, and that should put you on the scent of the probability of there being incipient colitis.

I will show you a case which happened to come up to my out-patients' quite recently. He is æt. 33 years, and has had nervousness for a long time, with tremblings all over, "palpitations," and feelings of faintness and giddiness. He was very weak in his walking. It appears that he came to my out-patients' previously for the same symptoms in 1903. but that was at a time when I was away. He came on account of the same shivering feelings, nervousness, and giddy symptoms. My notes say he is depressed, and has a flickering feeling in the epigastrium and a rising in his throat, causing him to catch his breath. The note says he feels weak, and starts suddenly when he falls off to sleep—another symptom of toxæmia. He works by gaslight all day. He came to the hospital the second time on March 14th. One cannot adopt heroic treatment for out-patients. I found that he had dyspeptic symptoms—fulness after meals. I put him on cascara sagrada 10 ℥, bromide of ammonium 10 gr., and mist. gentian alk. 3 ℥, one hour before meals. His teeth were not very good, though there was no pyorrhœa. I knocked off his meat, which is very difficult of mastication; also his sugar, which is one of the most fermentative of the gastric and intestinal contents. He is a cigar maker. He has now ceased smoking altogether, but previously he did not smoke more than two ounces of tobacco a week and an occasional cigar. After eight weeks' treatment he is not now nervous, and the trembling feeling has left him altogether. He felt nervous when crossing the road but not now. He has had medicine regularly, and has dieted from March 11th to the present time, and feels a different being. Such cases are very numerous. There are many other instances of toxic conditions causing neurasthenia did time permit.

But I want now to refer to the interesting question relative to the relationship between Graves' disease and neurasthenia. At the Nerve Hospital we get a considerable number of cases of Graves' disease on account of the nervous symptoms. Four groups of symptoms are met with in Graves' disease: proptosis and its consequences, thyroid enlargement,

* Clinical Journal, January 9th, 1907.

the vascular symptoms, and the neurasthenic symptoms. I think the neurasthenic symptoms are never absent. But of course it will be open to you to say that is because they all come to you on account of nerve symptoms. They do come to us for nerve symptoms, and therefore I suppose one notices that they are most constant. This patient is æt. 24 years, and she has been under my care for a considerable time—about a year. She came complaining of nervousness of six years' duration. She has been much worse during the last three or four months. There is no family history of any neurosis. Her appetite is good, but she feels very depressed. There are fine tremors in the outstretched arms. You notice the swelling of her neck; her thyroid is enlarged, and she has got tremor and nervousness, also palpitation and tachycardia. There is no cardiac enlargement, nor is there proptosis. I think it is a case of true Graves' disease, although there is no marked proptosis, and I think in her the nervous symptoms are an evidence of the toxic condition produced by the derangement of the thyroid secretion. The majority of cases of Graves' disease can, I believe, be so explained. You will notice in her a very interesting symptom, which puzzled me very much one time. She has got very well-marked nystagmus. I think that is congenital, and accidental to the case. Another view of the case is that it might be disseminated sclerosis, but she has not any of the other symptoms of that disease. Possibly the absence of proptosis may be related to the presence of nystagmus. I have treated her as a case of Graves' disease, but, as frequently happens in these cases, not always with great success. She has been in the hospital, and has had practically all the recognised treatments—rodagen, and the other preparation derived from goats, phosphate of soda, and various other drugs. She has also had X rays and the constant current; but, as I have said, not with very great succes. She went away to Paris with a friend the other day, and she has come back very much better! Here we have a thyroid toxæmia in operation which has produced symptoms of neurasthenia.

The next patient also exhibits Graves' symptoms. She is æt. 24 years, and she has for a considerable time had (1) tremors and various other symptoms pointing to the irritable nervous system which we call neurasthenia, such as nervousness and tremor of the hands; (2) tachycardia and shortness of breath; her pulse averages 140. For two years (3) her neck has been swollen, and (4) she had got proptosis. Von Graefe's sign is not present. She comes to us on account of (*a*) neurasthenia, and we find in her all the evidences of (*b*) Graves' disease. There is in her a third condition; when she first came (*c*) she had severe pyorrhœa alveolaris. The question is, What is the relationship between these three conditions? Have they any? It is very difficult to be quite sure about this. We know that neurasthenia or neurasthenic symptoms may be a consequence of the thyroid derangement we call Graves' disease. But, gentlemen, I have during the past two or three years, among hospital patients, seen five cases altogether in which these three conditions have been associated, and in which the cure or relief of the oral sepsis has been attended by an improvement in both the other two conditions, the neurasthenia and the symptoms peculiar to Graves' disease. This, I think, will turn out to be so in the present case. At first she had treatment directed to the Graves' disease without effect; latterly she has improved under treatment directed to the oral sepsis. The mouth has been put right, and she has had treatment and various remedies directed to the oral sepsis. Since May 6th she has been on styracol and castor oil, $\frac{1}{2}$ oz. at night. That is all one can say about the relationship of those three conditions at the present moment. In the series of cases I have referred to I feel almost certain that the oral sepsis was the cause both of the neurasthenic symptoms, on the one hand, and the swelling of the thyroid gland and the other symptoms proper of Graves' disease on the other, because they have all disappeared gradually under treatment directed to the former. She is still under treatment and the improvement is still going on.

July 19th, 1909.

A COPY of the third edition of Mr. P. Lockhart Mummery's manual on 'The After-treatment of Operations' has been sent to us by the publishers, Messrs. Baillière, Tindall and Cox, of Henrietta Street, Covent Garden. Mr. Mummery has added an excellent article on the serum and vaccine treatment of sepsis and has revised and brought up to date the chapter on shock.

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FAMILY JAUNDICE.

A Clinical Demonstration at the Medical Graduates' College and Polyclinic.

By ROBERT HUTCHISON, M.D., F.R.C.P.,
Physician to the London Hospital.

GENTLEMEN,—I want to show you this afternoon two cases which illustrate very well a rare and interesting condition which some of you may not have had an opportunity of seeing before, namely, family jaundice or congenital family cholæmia.

Family jaundice is a condition which has only been described within the last ten years or so, but like many diseases which are believed to be rare, when once it comes to be generally recognised it will probably be found to be not so rare as was supposed.

The main features of the disease are easily indicated: (1) It is characterised, as its name will tell you, by the presence of jaundice. (2) The jaundice is usually congenital. (3) It runs in families, occurring in successive generations and often in several members of the same generation. (4) There is enlargement of the spleen and sometimes of the liver also. (5) The blood shows marked changes, there being a diminution of the red cells and hæmoglobin and the presence of nucleated red cells, both normoblasts and megaloblasts. (6) Bile-pigment is present in the serum, but is usually absent from the urine, which, however, exhibits the presence of urobilin in excess. I shall show you immediately two patients who exhibit all these features in a well-marked form, the family history of whom is of considerable interest. Starting from their father, he was jaundiced all his life. His brother was also "yellow." There were therefore two members of that generation who were jaundiced. The mother of those two, that is to say, the grandmother of my patients, was also jaundiced. Her father's condition was doubtful, but he suffered at least "from his liver" all his life

The father of my patients had a largish family, of whom three are boys, all normal. There is one girl who is also unaffected. Then come the two patients I shall show you, both girls. Between them there was a boy, who died in infancy. He was born "yellow" and had an enlarged spleen when ten months old, so that he also was probably affected. Neither of my patients is married, and therefore we cannot trace the family tree any lower down. But, as I have indicated, we have here three generations that have been shown to exhibit jaundice in certain of its members. I shall now demonstrate the patients to you and then we will discuss the pathology, diagnosis, prognosis and treatment of the condition.

CASE 1.—This is the elder of the two patients; she is aged 27 years. You will see that she is a well-developed girl, but on looking carefully at her you will have no difficulty in seeing that her face is distinctly jaundiced and her conjunctivæ definitely though not deeply yellow. She has been that colour all her life; she was born yellow and has remained yellow. At times she is much yellower than she is just now owing to exacerbations of the jaundice.

There is another interesting point about this girl. Ever since she was eleven years old she has had attacks of pain in the upper part of the abdomen almost exactly resembling the pain of gall-stone colic. After these attacks she is for a time more profoundly jaundiced than before. Otherwise she is a healthy and active girl who has had no important illness. She exhibits a spleen which is enlarged half-way down to the umbilicus. She has a liver which can be felt to be slightly enlarged, hard and irregular. The urine in her case is highly coloured and always contains lithates; it contains a good deal of urobilin but no bile-pigment. Such cases are spoken of as "acholuric jaundice," because they are without bile-pigment in the urine. Had this been an ordinary case of jaundice one would, of course, have found bile-pigment in the urine.

As to the blood of this patient you are now looking at, she has a distinct though not an extreme degree of anæmia; she has 3,937,000 red cells, 80 per cent. of hæmoglobin, a normal number of white cells and several nucleated red cells, both normoblasts and megaloblasts—in other words, her blood exhibits those features which, as I have told you, are characteristic of family jaundice. The blood-serum gives the reactions for bile-pigment.

CASE 2.—The younger patient is aged 21 years, and she also has been yellow from the time she was born, although in her the jaundice is very much less pronounced than in her sister. Indeed, she looks almost more like a case of chlorosis than one of actual jaundice. She has had none of those attacks resembling biliary colic. She exhibits a greater enlargement of the spleen than her sister and a more profound degree of anæmia, although the blood changes are of the same kind. Her urine is clear and contains urobilin but no bile-pigment. I should add that in both these cases bile-pigment is present in the stools in a normal amount.

I shall now exhibit to you this second patient, and shall demonstrate the enlarged spleen in her. You will see at once that she has a very different tint from her sister, although she is very far from being of a normal colour. The conjunctiva is scarcely jaundiced in the proper sense at all; it is slightly lemon-coloured perhaps. The skin of the face has more the tint of chlorosis than that of true jaundice. However, there is no question of her really being jaundiced, because bile-pigment is present in the blood-serum though absent from the urine. After examining the abdomen you will see that there is no doubt about the enlargement of the spleen. It reaches to about two fingers' breadths above the umbilicus, and the liver can be felt to about the breadth of one and a half fingers below the costal margin and is slightly irregular. It is curious that, like most cases of the family form, these patients do not suffer from other symptoms common in ordinary jaundice. They do not get the slow pulse or itching of the skin, in fact the jaundice does not seem to incommode them much at all except by being unsightly.

Pathology.

I wish to speak next of the pathology of family jaundice. There are, as you know, two varieties of jaundice. There is, first, what you may speak of as obstructive jaundice, and secondly, there is what is sometimes spoken of as non-obstructive jaundice and sometimes as hæmatogenous jaundice, for reasons that we shall see immediately. Obstructive jaundice is characterised by

the fact that bile is absent from the stools, and it is due to an obstruction in the chief bile-ducts. In both these patients bile is not absent from the stools, and therefore we can say that they are not examples of obstructive jaundice in the ordinary sense. So we are compelled to regard them as cases of hæmatogenous jaundice or jaundice due to an increased destruction of blood.

You may ask, "What evidence have we here to support the view that the jaundice is hæmatogenous?" Well, in the first place, there are the characteristics of the blood itself. The patients are distinctly anæmic, particularly the younger one, who has only about 2,000,000 red cells and a very low amount of hæmoglobin. Such anæmia is in keeping with the view that there is an increased destruction of blood.

Secondly, the presence of nucleated red cells is in keeping with that view, because it indicates that the bone-marrow is doing what it can to make good the increased destruction of red cells. Just as in pernicious anæmia, where there is increased destruction of red cells, both normoblasts and megaloblasts are found in the blood-stream, so here the presence of nucleated forms argues an increased destruction of the blood.

In the third place there is direct evidence that in these patients the red blood-corpuscles are unusually fragile. It has been found by many observers that in family jaundice the red blood-corpuscles are unusually easily broken down or hæmolysed.

Examining the blood of the patients I have shown you from that point of view, it was found that the red cells are broken down by a dilution of normal salt solution which does not affect the red cells in an ordinary person—in other words, they break down too easily; they are unusually fragile. You may ask, To what is this fragility due? It might be due to something present in the blood serum which makes them fragile and breaks them down easily. But if you take the blood-serum and try it with ordinary red blood-corpuscles you find that it does not affect them at all. So that the breaking down of the red cells has nothing whatever to do with the serum. Again, you might say that possibly people who have remained jaundiced for a long time from any cause would present this condition of fragility of their red cells, but I have examined the blood of a woman who had had obstructive jaundice from gall-stones for three years and her red cells did not show any great tendency to break down. One is therefore driven to the conclusion that the increased fragility of the red cells in these cases is a congenital peculiarity, which in all probability is inherited. According to this view family jaundice is not truly a disease of the liver at all, it is a disease of the blood-forming organs; it is really a blood disease. The subjects of it are born with red cells which are abnormally fragile, and this peculiarity is handed down from one generation to another. When the red cells break down an excess of blood-pigment is thrown into the circulation to be dealt with, and being more than the liver can properly handle the result is that the bile is unduly viscid, it stagnates in the bile-capillaries, and some of it is absorbed into the blood-stream.

That, then, is the generally accepted view of the pathology of these cases, but I freely admit that there are still some difficulties. The chief of these is to understand why it is that although these patients get bile-pigment in the blood they do not get it in the urine; why it does not leak through the kidney as in ordinary cases of obstructive jaundice. It may be because there is too little bile-pigment to get through the kidney, but after all one of these girls is as yellow as a great many people with catarrhal jaundice who do have bile-pigment in the urine. You must not suppose, however, that in all cases of family jaundice bile is absent from the urine. Usually it is so, but in a few it has been present. Why some cases should be acholuric and others not we do not know.

Prognosis.

Now as regards the course and prognosis. As I have told you, the disease is congenital, but the patients may live fairly healthy lives and attain a good age. One of the recorded cases lived to above eighty years of age. The father of my patients lived to fifty-nine and the grandmother lived longer than that. If women, they are apparently able to have children without risk. So that the prognosis is not unfavourable as regards the effects of the disease upon the patient's longevity, nor is it unfavourable as regards the effects of the malady in predisposing to other diseases, with the possible exception of gout, or in complicating other diseases.

Diagnosis.

With regard to the diagnosis, if you meet a well-marked case and get a clear history there should be no difficulty in coming to a proper decision.

On the other hand, some cases may give rise to difficulty in the absence of a good history. When I first saw the younger of these two patients, for instance, I thought she was suffering from splenic anæmia. At that time she had more anæmia than now and she was scarcely jaundiced at all, and had a large spleen and blood changes which were compatible with splenic anæmia. So that you must bear in mind the possibility of the blood side of the picture being so prominent and the jaundice side so slight as to lead you to a wrong conclusion. The moral, therefore, is that in all cases of chronically enlarged spleen one should go into the family history with great care, because a diagnosis of splenic anæmia might lead to grave errors in treatment. I seriously considered for some time having the spleen removed from the younger of these patients, believing that I was dealing with splenic anæmia. But in a case of family jaundice as she really was, such a procedure would have been full of danger.

Treatment.

With regard to treatment, you can easily see that if the accepted view of the pathology of the disease be correct there cannot be very much to be done. It must be very difficult to lessen the destructibility of the red cells, and yet that is just what we want to do if we are to strike at the root of the affection. Treatment by remedies such as arsenic and iron, that ordinarily do good in other blood disorders, have not been found to have any appreciable effect in these patients. In one recorded case drainage of the gall-bladder was carried out under the belief that there was a chronic infection of the bile-passages, but the results were not satisfactory. I treated the younger of these patients by the passage of the X rays through the spleen for six months, being under the impression, at that time, that I was dealing with a case of splenic anæmia. The spleen certainly became smaller and harder and her general health improved somewhat, but the gain has not been striking. The elder sister I have treated with small doses of salicylate of soda, and it is a striking fact that since she began that treatment she has had no recurrence of the severe attacks of pain which she used to suffer from. Whether the benefit is going to be permanent I do not know, but she is distinctly better. Considering, however, that the disease has no bad effects as far as we know on the patient's chances of life, the question of treatment is really more a cosmetic one of improving the appearance than a matter of any real importance.

July 26th, 1909.

DISEASES OF THE THYROID GLAND.

A Debate held under the auspices of the Hunterian Society.

Dr. ARTHUR T. DAVIES, President, in the Chair.

THE RELATIONSHIP BETWEEN GRAVES' DISEASE AND DIABETES.

By GEORGE R. MURRAY, M.A., M.D.Camb., D.C.L Durh., F.R.C.P.,

Professor of Systematic Medicine, Victoria University of Manchester; Physician to the Manchester Royal Infirmary; Consulting Physician to the Royal Victoria Infirmary, Newcastle.

WHEN I first received the kind invitation of your secretary to open a discussion on diseases of the thyroid gland I was in doubt as to what aspect of the subject I should deal with in order to avoid, as far as possible, going over ground with which you are already familiar, so I decided that we might with advantage discuss the relationship of the thyroid to some of the other secretory glands in the body. The purely local diseases of the thyroid, which do not cause any marked alteration in its secretory activity, do not appreciably affect the functions of the other glands. Other glands may, however, be profoundly affected by the loss of function of the thyroid, as in myxœdema and cretinism. In illustration of this I need only mention the sweat-glands, which practically cease to act when the normal stimulus supplied by thyroid secretion is wanting. It is, however, of the results of excessive thyroid secretion in association with exophthalmic goitre, and its action on the function of other glands, that I wish to speak on this occasion.

There is good reason to suppose from recent observations that internally secreting glands do not act as so many isolated units, but that they exert a considerable amount of influence upon each other, possibly somewhat in the same way as do the digestive glands. Thus, in addition to the important part which thyroid secretion plays in general metabolism, and especially in the oxidation of the tissues, it appears to influence the secretory activity of other glands in a special manner, so that any modification of the function of the thyroid

may affect other glands as well. It is now generally accepted that in exophthalmic goitre there is a greatly increased secretory activity of the thyroid gland, so that in some cases of this disease we have the opportunity of observing the results of the action of this on other glands in the body. In illustration of this I propose to consider the pancreas and the pituitary gland. The internal secretion of the pancreas is probably furnished by the islands of Langerhans. When these fail or are removed by excision of the pancreas, severe diabetes results. In acromegaly the pituitary body is enlarged and hypertrophied, and there is good reason to believe that excessive secretion of this gland is the important factor in the production of this strange malady. My attention has been drawn to the relationship between the thyroid gland and the pancreas by a group of four cases which have come under my observation, in which exophthalmic goitre has been accompanied or succeeded by a severe form of diabetes. I will give you the main features of one case in which an autopsy was made, and allude briefly to the other three, as they serve to illustrate the point I wish to raise for discussion as to the relationship between the two diseases. It seems probable that the abnormal activity of the thyroid gland in exophthalmic goitre is the cause of the alimentary glycosuria which occurs in some cases, and under certain circumstances has such an adverse effect upon the pancreas as to lead to the development of a severe and fatal form of diabetes.

E. M—, a single woman, æt. 20 years, was under my care as an in-patient at the Newcastle Royal Infirmary from December 22nd, 1903, to March 22nd, 1904. She had enjoyed good health until two years before her admission, when she had some swelling of the legs. Prominence of the eyeballs had first appeared eighteen months before her admission. Six months later some enlargement of the thyroid gland was first noticed, which gradually increased until it caused some difficulty in breathing. She had always been rather nervous and liable to palpitation, but became more so during these two years. The weight had decreased by 21 lb. during eighteen months.

On admission she was emaciated; there was well-marked exophthalmos associated with retraction of the upper eyelids and von Graefe's sign. The thyroid gland was symmetrically enlarged, the pulse frequency was 125, and a systolic murmur was audible at the apex. There was a fine tremor of the hands, and the skin was moist.

During her stay in hospital she was treated with a special serum and by electricity. She improved in general condition and gained 7 lb. in weight, otherwise there was no marked change in her condition at the end of the three months. Unfortunately no note as to the condition of the urine can be found. As no special note was made of the fact, sugar was almost certainly absent at that time.

Four years later, on March 12th, 1908, she was readmitted to the hospital complaining of great thirst which had troubled her for twelve months, during which, in spite of diet and treatment, she had lost 2 st. in weight. On examination only a slight enlargement of the thyroid gland could be felt. From the time of her admission until her death on June 11th the frequency of the pulse was generally about 70, 80 and 52 being the highest and lowest pulse-rate observed. No murmurs were audible. There was no tremor of the hands, so that the symptoms of Graves' disease had subsided. She was pale and thin, and complained of thirst, which was less severe than it had been. The appetite was variable. The skin was dry, and had lost much of its natural elasticity.

During March the amount of urine passed in the twenty-four hours varied from 22 to 86 oz. The specific gravity was from 1038 to 1050. The smallest quantity of sugar excreted was 432 gr., and the largest 1694 gr. *per diem*.

During April, while the patient was on a strict diet and was taking codein 1½ gr. thrice daily, the daily amount of urine varied from 30 to 112 oz., the specific gravity from 1041 to 1052, and the total amount of sugar from 270 to 1222 gr.

During May and up to June 9th the quantity of urine varied between 64 and 126 oz., the specific gravity from 1030 to 1044, and the total amount of sugar from 697 to 3759 gr.

She gradually got worse, and died on June 11th. Towards the end the urine gave the diacetic acid reaction with perchloride of iron. The post-mortem examination was made by Dr. George Hall, to whom I am indebted for the following notes:

"The body is thin, *rigor mortis* is beginning, the blood is of a chocolate colour when it first appears from the cut veins; later on standing, a

well-defined creamy layer appears floating on the surface. The right ventricle on being incised shows a loose, colourless clot and pale, somewhat milky, fluid around.

"*Heart* of normal size, flabby; a small patch of thickened exocardium on the anterior surface of the right ventricle. Mitral orifice and valve normal.

"Aortic valve normal; there is a little fatty change in the endothelium of the early part of the aorta; the tricuspid orifice and valve are normal; muscle substance of right side very flabby.

"*Lungs.*—Both are small; the upper lobes on the two sides are slightly pale, but the tissue on section is normal; at the base on both sides there is some little congestion and a little collapse; some adhesion by recent lymph between the middle and lower lobes (right); no evidence of tubercle.

"*Liver* of normal size; shows some patchy fatty appearance on the surface; on section there are areas of pallor of a fatty character where lobulation fairly distinct, but, taken as a whole, the lobulation is indistinct.

"*Spleen* of normal size; the capsule and pulp show no gross change of an abnormal type.

"*Kidneys* average size, the capsule strips easily leaving a smooth surface; the cortex is of normal thickness, but pale in parts.

"*Pancreas* shows no great change, but in some parts appears to be rather more fibrous than is usual."

On microscopical examination the thyroid gland does not show the characteristic changes which are seen in the active stage of Graves' disease.

The alveoli vary in size, some being considerably larger than in the normal gland. The larger alveoli have evidently been formed by the fusion of several smaller ones, as the remains of the intervening septa can be seen here and there projecting into the lumen of the alveolus. Only here and there can the remains of a slight plication of the alveolar wall be made out. Otherwise the alveoli are normal in appearance, they are well filled with colloid, and the lining epithelium is of the normal cubical type.

In the pancreas there is a distinct increase in the amount of the connective tissue throughout the section, and the islands of Langerhans have practically disappeared.

In this case the patient recovered from a typical attack of Graves' disease, which was, however, followed by a severe form of pancreatic diabetes to which she succumbed. The disappearance of the Graves' disease was evidently due to the return of the thyroid to a normal condition, and is an interesting example of how complete this recovery of the gland may be. The diabetes was the result of the destruction of the islands of Langerhans. I shall briefly refer to the other cases before we consider the significance of this association.

M. S—, a married woman, æt. 25 years, who had borne two children, was admitted under my care at the Newcastle Infirmary on May 23rd, 1905. At the age of sixteen she had received a severe shock, as a young man with whom she was riding on a "switchback" was thrown out and killed. After this she suffered from "fits," which appeared to have been hystero-epileptic attacks and recurred at intervals up to the time of her admission. For two years she had noticed a swelling in the front of the neck and prominence of the eyeballs. She became more nervous, lost nearly a stone in weight, the hair had been coming out, the skin became moist, and she perspired freely at times. On admission there was slight enlargement of the thyroid gland, but there was no thrill or bruit over it. The neck, face, and especially the eyelids were pigmented. There was general nervousness with well-marked tremor of wider range than usual, which affected both hands and feet. The skin was moist. Slight exophthalmos, retraction of the upper eyelids and von Graefe's symptom were present. There was slight external strabismus of the right eye, and the sight of this eye was so defective that she could only distinguish light from darkness. There was nystagmus on looking to the left. On ophthalmoscopic examination the left fundus was normal in appearance, but there was detachment of the retina in the right eye. There were definite visual hallucinations at night. The pulse was 124, regular. The cardiac impulse was diffuse, and faint systolic murmurs were audible at the apex and also over the pulmonary area. The urine at this time was acid, had a specific gravity of 1026, and contained neither sugar nor albumen. She was in the hospital for three weeks and was then discharged. Nearly three years later, on April 2nd, 1908, she was again admitted, and stated that she had suffered from general weakness and thirst, and had been passing a large amount of urine for a year. During

these twelve months the weight had decreased from 10 st. to 7 st. 6 lb. On admission she still had very slight exophthalmos, there was no visible enlargement of the thyroid gland, but on palpation it appeared to be slightly larger than normal. The skin was dry, and there was marked constipation. She complained of occasional attacks of pain in the cardiac region, which were liable to occur after exertion. The pulse, during her stay in hospital, varied between 72 and 100, the higher rate being noted only on one occasion.

The urine contained sugar, which, however, varied considerably in amount during her stay in hospital. No diacetic acid reaction was obtained on testing with perchloride of iron solution. During the month of April the urine passed in twenty-four hours varied in amount between a minimum of 28 oz. on April 7th and a maximum of 160 oz. on April 28th. The smallest amount of sugar passed during this period was 385 gr. on April 14th, and the largest amount 2800 gr. on April 28th. During the month of May the daily amount of urine was further increased, the smallest amount being 130 oz. on May 3rd, and the largest 416 oz. on May 28th. The smallest quantity of sugar passed in one day was 1690 gr. on May 3rd, and the largest 6510 gr. on May 12th. Up to June 17th the smallest amount of urine was 328 oz. on that date, and the largest quantity 416 oz. on June 5th and 8th. The smallest amount of sugar on any one day was 5108 gr. and the largest 6022 gr. These figures without further detail are sufficient to indicate the severity of the diabetes even when treated by a suitable diet and the administration of codein. When this case was first under observation she was suffering from exophthalmic goitre without glycosuria, whereas three years later she had practically recovered from the exophthalmic goitre, but was suffering from a severe form of diabetes.

Mrs. D—, æt. 38 years. At the age of twenty-five there was some slight enlargement of the thyroid gland associated with exophthalmos, which subsequently disappeared. When she was twenty-nine she took thyroid tablets for a few weeks, and the former symptoms returned and she also had a good many severe "anginal" attacks. When first seen at the age of thirty-eight there was considerable uniform enlargement of the thyroid gland, there was marked exophthalmos and pigmentation of the eyelids, other ocular symptoms being absent. The pulse was 120; the apex-beat was in the fifth space in the left nipple-line, and systolic murmurs were audible at the apex and over the pulmonary area. She was very nervous; the skin was moist and at times there were sweats. The urine had a specific gravity of 1025 and contained 15 gr. of sugar to the ounce, 1650 gr. being passed in the twenty-four hours; no diacetic acid was present. There had been a loss of weight amounting to 3 st.

When seen about thirteen months later she had gained a stone and weighed 7 st., but the urine contained diacetic acid. The pulse was still 120. Four months later the weight had fallen to $5\frac{1}{2}$ st., she was suffering from syncopal attacks, and the pulse was 104. About a year later she died from diabetic coma.

We have here a case of exophthalmic goitre, which apparently recovered, but relapsed on taking thyroid tablets, the second attack persisting and becoming complicated by the development of composite diabetes.

G. T—, a man, æt. 22 years, was first seen in August, 1898. At the age of sixteen he had had scarlet fever, followed by general œdéma which lasted for twelve months, and was presumably due to a nephritis. The œdema had reappeared eighteen months before he came under observation. One sister, after scarlet fever, developed exophthalmic goitre, from which she afterwards entirely recovered. While he was under my observation for a short time in 1898 he had a goitre of moderate size, which had been present for nine months, some exophthalmos and a very slight tremor. The urine contained no sugar, but there was a trace of albumen. The pulse varied between 76 and 100, and on one occasion while he was suffering from a slight tonsillitis without any fever it was 130.

In July, 1908, ten years later, he was admitted to the Newcastle Infirmary complaining of great thirst of one month's duration. After the onset of the thirst he had frequent micturition, and steadily lost weight and strength. Previously he had suffered more or less from palpitation, he had been rather nervous, and had perspired freely.

On admission he was found to be very thin. The thyroid gland was not much enlarged and there was a small adenoma in the right lobe. The

eyes were slightly prominent, but not so much so as they had been ten years before. The pulse was 112 and irregular. The apex-beat was in the sixth left intercostal space, half an inch internal to the nipple line. A systolic murmur was audible at the apex and was conducted out to the mid-axilla. A large quantity of urine was being passed, amounting to as much as 232 oz., containing 5800 gr. of sugar in the day. After treatment the amount of urine diminished to between 136 and 172 oz., and the daily quantity of sugar varied from 3360 to 3612 gr.

In this case we have an example illustrating the development of diabetes nearly eleven years after the onset of Graves' disease.

We have here a group of four cases of exophthalmic goitre, one being in a man and three in women, in which severe diabetes developed at a variable interval after the exophthalmic goitre had first appeared. In each case the symptoms of exophthalmic goitre had either subsided or decreased considerably by the time the diabetes had declared itself.

This association of diabetes with exophthalmic goitre has been recorded by several different observers. In 1874 Sir Lauder Brunton* described a fatal case in which both diseases were present at the same time, and in the following year a similar case was published by Sir Samuel Wilks,† in which the diabetes developed some six months after the onset of the Graves' disease; and a third case was recorded by O'Neill ‡ in 1878.

In some recorded cases the Graves' disease has developed in a patient already diabetic, in others the two diseases have run concurrently, while in a third group, to which my own cases belong, the diabetes has followed the onset of the exophthalmic goitre after a variable interval. A comprehensive survey of the subject was made by H. Stern,§ who quotes the observation of Chvostek, who found alimentary glycosuria in 69 per cent. of his cases of Graves' disease—a much larger proportion than is seen in this country. In eight cases of Graves' disease Stern succeeded in inducing an alimentary glycosuria in only one. After the ingestion of 75 grms. of grape-sugar 3·3 grms. were excreted in the urine, so that the limit of assimilation was hardly passed.

In the case of Graves' disease with diabetes observed by Stern in 1901 there had been a previous attack of Graves' disease in 1898, which had subsided after (and in spite of) a course of thyroid treatment. The recurrence in 1901 was accompanied by diabetes, and on this occasion the administration of thyroid powder with arsenic caused a rapid increase in the amount of sugar in the urine, from 25 grms. to 35, 60, 67 and 46 grms. in four succeeding days. This case ended fatally. Altogether Stern collected twenty-four cases of combined exophthalmic goitre and diabetes, twenty-two of which were in women and two in men. The youngest was eighteen and the oldest fifty-nine. Ten of the twenty-four had died under observation. I agree with him that in those rare cases in which exophthalmic goitre has developed in a patient already diabetic the association is probably a coincidence only, so that we are only concerned with those in which the diseases are concurrent or the diabetes is secondary to the Graves' disease.

This sequence of events is, I believe, more than a mere coincidence, and this view is supported by certain experimental observations to which I shall briefly refer.

Experimental evidence indicates that the diabetes may be a direct result of the Graves' disease.

H. Eppinger, Falta, and C. Rudinger* show that there is a direct relationship between the thyroid gland and the pancreas, and that these two glands tend to inhibit each other, so that an increase of function in the thyroid gland leads to a diminution of function in the pancreas, while a diminution in the activity of the thyroid permits an increase to take place in the functional activity of the pancreas.

As a result of the hyperthyroidism which occurs in Graves' disease there is, in addition to increased proteid and fat metabolism, an inhibition of the pancreas which causes a relative insufficiency of its internal secretion. This results either in actual alimentary glycosuria or in a condition in which glycosuria is readily induced by an excessive carbohydrate diet.

A similar result has been observed in the hyperthyroidism artificially produced by means of thyroid

* 'St. Bartholomew's Hosp. Rep.,' vol. x, 1874, p. 253.

† 'Lancet,' 1875, p. 371.

‡ *Ibid.*, March 2nd, 1878, p. 307.

§ 'Journ. of the Amer. Med. Assoc.,' vol. xxxiv, 1902, p. 972.

* 'Zeitschrift für Klinische Medizin,' 66, 1908, p. 1.

feeding. Thus Bettmann gave thyroidin or iodothyrin for a week to twenty-five healthy persons, and with the last dose he gave 100 gr. of glucose. He induced glycosuria in twelve. In each case the glycosuria subsided in a week.

Dr. Hector Mackenzie* also states that the amount of carbohydrate which can be taken without causing glycosuria is less than the average, both in Graves' disease and in hyperthyroidism induced by excessive thyroid feeding in man and in dogs.

Not only may the hyperthyroidism induced by administering large doses of thyroid extract be accompanied by glycosuria, but in a few cases it is stated to have been followed by the development of true diabetes. In myxœdema, on the other hand, as might be expected, a larger amount of grape-sugar than normal can be absorbed without the occurrence of glycosuria.

Lorand,† who has drawn attention to this relationship between pancreatic and thyroid disease, has found that in a dog examined three days after thyroidectomy sections of the pancreas showed already an apparent increase in the islets of Langerhans, indicating that the elimination of the thyroid control was followed by increased pancreatic activity. He also found that in dogs rendered diabetic by the removal of the pancreas, the glycosuria either almost or entirely disappeared after a subsequent thyroidectomy, though the animal only survived the second operation for a short time.

This occurrence of diabetes as a complication or late sequel of exophthalmic goitre is therefore of much interest, and we require much fuller information as to the frequency of this sequence. I would suggest that the pancreatic disease is possibly the outcome of a prolonged inhibitory action of the excessive amount of thyroid secretion present in the blood-stream in Graves' disease, which in the first instance causes only an alimentary glycosuria, but in time leads to atrophy and fibrosis of the pancreas and more especially of the islands of Langerhans, and in this manner in certain predisposed subjects leads to the establishment of a severe and fatal form of diabetes.

* Allbutt and Rolleston's 'System of Medicine,' vol. iv, pt. 1, p. 331.

† 'Comptes Rendus des Séances de la Société de Biologie,' t. lvi, p. 488.

Laignel-Lavastine* has recently collected many interesting observations, which tend to show that there is reason to suppose that there is a considerable degree of co-relation between the internal secretory glands, into the consideration of which time will not permit me to enter. I wish, however, to draw attention to an interesting group of cases allied to those which we have just considered, in which combined disease of the thyroid gland and of the hypophysis may occur and be associated with diabetes. Some years ago I recorded two of these cases.† One was a single woman. æt. 37 years, who suffered from typical acromegaly. She also had a goitre, frequent pulse varying from 128 to 140, exophthalmos and tremors. The urine had a specific gravity of 1035 and contained 40 gr. of sugar to the ounce. She had pulmonary tuberculosis as well.

The other case was that of a widow who also had typical signs of acromegaly; the pulse varied from 100 to 132, the urine was abundant, had a specific gravity of 1040, and contained a considerable amount of sugar. She also developed phthisis. At the autopsy the pituitary gland was considerably hypertrophied, the thyroid gland was enlarged, weighing nearly 2 oz., and the thymus was persistent and the left lobe hypertrophied.

Cases have also been recorded by Lancereaux‡ and by H. Henrot, of acromegaly associated with exophthalmic goitre and diabetes in the same person.

Thus, of my own cases six have suffered from exophthalmic goitre and diabetes and two of them had acromegaly as well.

Lorand,§ who has drawn attention to this remarkable relationship between Graves' disease, acromegaly and diabetes, considers that in these cases the diabetes is due to the excessive activity of the thyroid gland, which induces the changes in the islands of Langerhans which are the immediate cause of the diabetes.

From these various observations we learn some practical lessons. First, it is obvious that when diabetes occurs along with or subsequently to

* 'Gazette des Hôpitaux,' November 14th, 1908, No. 131, p. 1563.

† 'Edinburgh Medical Journal,' February, 1897, p. 170.

‡ 'La Semaine Medicale,' 1895, p. 61.

§ 'Comptes Rendus des Séances de la Société de Biologie,' t. lvi, p. 554.

exophthalmic goitre, the prognosis is a grave one, as cases which would in all probability have recovered from the exophthalmic goitre alone die from the diabetes. Secondly, it appears that thyroid extract should not be given to patients suffering from diabetes, as it may aggravate the symptoms. Thirdly, the urine should be carefully examined for sugar from time to time in all cases of Graves' disease, and if any glycosuria appears it should be promptly treated by suitable dieting, as it is possible that by prompt early treatment of the glycosuria we may prevent, or at any rate postpone, the onset of actual diabetes.

Mr. WALTER EDMUNDS said he would confine himself to the treatment of Graves' disease. As some enlargement of the thyroid gland seems to be a fairly constant condition in the disease, and as the microscope shows the gland to be in a state of activity, it may be inferred that the increased and possibly altered secretion of the thyroid plays an important part in the causation of the symptoms. The most obvious method of reducing the secretion is by the removal of a portion of the enlarged gland by operation. This procedure has unfortunately been accompanied by a heavy mortality in the past, but in those cases which survive there has generally been much benefit. In one case in which I operated all the symptoms, including periodic attacks of dyspnœa, were greatly relieved, and the patient almost cured. It would seem that the mortality is in some way connected with the late stage at which the operation has been decided on. If the case is to be treated in this way the operation should be performed at a comparatively early stage.

A second mode of treatment consists in the administration of what may be considered an antidote to the secretion. It is supposed that in the normal animal the thyroid secretion is neutralised by another body, called anti-thyroidin. If, then, the thyroid gland is excised, the anti-thyroidin would be left free and available to neutralise the excessive secretion from the thyroid of Graves' disease. The anti-thyroidin can be administered in the blood-serum either liquid or dried, or in milk either fresh or dried. I have made a trial of this treatment, using the fresh milk of thyroidless goats. The results have been recently published ;* they seem to me encouraging. In one case, which had been in hospital some weeks and was steadily getting worse, a marked improvement followed the administration of the milk, and the patient was almost completely cured. In another case it is true the whole of the milk from a goat was given during two consecutive summers, and the patient is now as bad as at first, but it must be remembered that she might have been worse had not the milk been given.

A third method of treatment is by the application of X-rays ; these seem to have a special action on newly-formed tissue, and might be expected to reduce the goitre. Dr. Hector Mackenzie tells us he has given this treatment a fair trial, but with disappointing results. Recently, however, Mr. Thurstan Holland, as the result of his experience, says that "he has no doubt in his own mind that the judicious administration of X rays is of the greatest value in exophthalmic goitre."* He records one case in which the patient, although under treatment in hospital for weeks, was getting worse, but who greatly improved on the administration of X rays ; the physician under whose care the case was expressed the opinion that the rays had saved the patient's life.

The last method of treatment to be referred to is the administration of calcium. It seems fairly certain that Graves' disease is not due to an affection of the parathyroid glands ; they have been found normal in the disease ; also while the removal of the parathyroids causes well-marked destructive changes in the nervous system, no such definite pathological changes can be found in Graves' disease. The symptoms, too, of Graves' disease differ widely from those produced by parathyroidea. Tremors are, however, common to both, thus it is possible that the parathyroids may be concerned with Graves' disease. Now, it has been shown on the continent and in America that the ill-effects produced by removal of the parathyroids may be greatly obviated by the administration of salts of calcium. I have recently made some experiments on this point. In one dog two thirds of one thyroid lobe was removed, leaving on that side one third of the lobe and a parathyroid. A few weeks later the opposite lobe with its parathyroids was excised ; the dog remained well. After another long interval the dog was placed on a milk

* 'Lancet,' January 25th, 1908, and April 10th, 1909.

* 'Proc. Roy. Soc. Med.,' March, 1909.

diet (as milk contains much calcium); also lactate of calcium was given. After a few days of this treatment the remaining third of the thyroid lobe together with the parathyroid was removed. Instead of the dog, as usually happens under these circumstances, dying quickly, he remained well for some time. Symptoms, however, came on late; these were treated with subcutaneous injections of lactate of calcium, each of which did much good, lasting about twenty-four hours, but the dog getting somewhat rapidly worse, an anæsthetic was given and 9 gr. of lactate of calcium injected into the external jugular vein. This completely removed the tremors and other symptoms, and the dog became, and is at present, well. By similar treatment I have saved another dog, and have now two dogs and two cats without either thyroid or parathyroid, whose lives have been saved, as I believe, by the calcium treatment. If, therefore, in Graves' disease, either without or after operation or in other thyroid operations in which the parathyroids have been exposed to injury, severe symptoms occur, it may be advisable to inject lactate of calcium intra-venously. Milk, no doubt, generally occurs in the diet of cases of Graves' disease, but lactate of calcium seems to act better, either by mouth or subcutaneously, and best intra-venously.

Dr. DAVID FORSYTH said: Since the day when the essential lesion in myxœdema was first recognised, no more important question bearing on the thyroid gland has been raised than that of the function of the parathyroids. These are small bodies, to the naked eye not unlike lymphatic glands, which are found in varying numbers in the neighbourhood of the thyroid. Histologically they have a distinctive structure, being composed of masses of polyhedral cells which actively secrete a colloid material. The suggestion has been made that these little glands possess an important function of their own, and must be taken into account in every problem associated with the thyroid. I propose, therefore, to discuss this subject. I shall then briefly put before you some considerations, suggested by an investigation of these glands, with regard to the pathogeny of goitre.

The relation between the parathyroids and the thyroid.—The belief, expressed by Sandström in 1880, that the parathyroids are merely embryonic rests is now shared by few, if any, modern workers. Recent investigations have led to the growth of two contrary views. Some hold that the parathyroids are independent of the thyroid, that their function is important in the highest degree, and that its suppression leads to a speedy death. This theory we may refer to as the vitally essential theory. Other observers, however, are satisfied that parathyroid tissue, though endowed with active secretory powers, represents a stage in the development of thyroid tissue; that it is, therefore, thyroidal in nature, and possesses no specific function. I shall briefly lay before you the evidence on which these beliefs are founded.

The vitally essential theory is based on the results of experimental removal of the glands. This operation has been performed very many times, and is often followed by symptoms suggestive of tetany, and may be fatal in a few days. Thus in a series of ten dogs from which Vassale and Generale* removed the parathyroids nine died within a fortnight. In Mr. Edmunds'† series of nine dogs three died within a week, one at the end of a month, but five survived the operation. Vincent and Jolly‡ found that in cats the operation was fatal in only 33 per cent. of their cases. These three series of experiments, which fairly represent the varying results obtained, prove that the operation is by no means always fatal. An explanation of this fact is obviously necessary before we can accept the theory. We might be tempted to assume that in the unsuccessful cases a parathyroid gland has accidentally escaped removal; but in order to carry weight this assumption mnst be confirmed by ocular demonstration of the missing gland. In the absence of this proof it would be unwise to base any conclusion on the experiment. Unfortunately the assumption, though often made, is rarely supported by this proof. If four parathyroids are removed and the animal dies—I quote an argument frequently used—we have proof of the essential nature of the glands. If, however, four parathyroids are removed and nothing happens, then we must conclude that a fifth parathyroid has been left behind, otherwise acute symptoms must have de-

* 'Arch. Ital. de Biol.,' Turin, 1896, xxv, p. 459, and xxvi, p. 61.

† 'Journ. Path. and Bact.,' 1900, vol. vi, p. 65.

‡ 'Journ. Physiol. Camb.,' vol. xxxii, p. 65, and vol. xxiv, p. 295.

veloped. I could give many instances of this reasoning (which is *petitio principii*), but one example must suffice. I take it from a paper just published by one of the most prominent exponents of the vitally essential theory.

In the January number of the 'Journal of Experimental Medicine' Prof. MacCallum thus accounts for the absence of any symptoms after he had excised the parathyroids from a dog.

At first operation four parathyroids were removed, but no symptoms of tetany appeared. On June 5th another operation was performed, but no parathyroid could be found. On June 17th both thyroid lobes were removed, and tetany appeared, showing that some internal parathyroid was extirpated together with the thyroid.

This method of reasoning can have no weight. If we are to draw any conclusion at all from this incomplete experiment it must surely be that the loss of the thyroid occasioned the tetany. Further, if we are to assume the presence of additional glands in cases in which the operation fails to produce acute symptoms, what is there to prevent us making the same assumption in those cases which are fatal? Is there not as much—or as little—justification for concluding that the acute symptoms develop even though the parathyroid function has not been suppressed? These cases in which no ill-effect follows are far too numerous to be set aside.

In other cases, however, the operation for parathyroidectomy is performed, and the animal does develop acute symptoms, and often dies. It is on these operations that we must rely for support to our theory. It will repay us to examine these experiments closely. Now, we shall find that the large majority of them have been made on the three following suppositions: that the parathyroids are four in number, that they bear a well-known anatomical relation to the thyroid, and that they can be identified with the naked eye. To test these points I recently made a detailed examination, anatomical and histological, of the glandular structures in the necks of many mammals and birds, from man downwards, and I ascertained the following facts.

The parathyroids are by no means always limited to four; there may be eight, ten, or even more. They are inconstant in position, and may lie at any level between the lower jaw and the base of the heart. Quite frequently portions of parathyroid tissue are attached to lymphatic glands, to thymic nodules, or to accessory thyroids, while they may even be buried deeply in the thyroid itself. Finally, the glands cannot be recognised with certainty, except by histological examination.

These facts obviously have a direct bearing on the results of operations planned on the three assumptions I have mentioned. Before an experiment can be claimed as a successful parathyroidectomy the glands removed must be identified under the microscope, for they may well be lymphatic or accessory thyroid. Post mortem, all the glands from the jaw to the aorta should be similarly identified. Finally, the thyroid itself must be sectioned for buried parathyroids.

In very few cases, however, has any examination been made of the glands removed by operation, still less of those left behind. Professor MacCallum, himself a believer in this theory, says that it is "difficult, if not impossible, for the operator to recognise every focus of parathyroid tissue," and he states that even after every possible structure which could shelter the tissue has been removed the animal may still remain quite well. The proof, therefore, of the serious effects of parathyroidectomy needs much strengthening before we can accept it.

The most recent experimental development in support of the theory has been made in another direction, namely, by transplanting one or more parathyroids and subsequently clearing out from the neck all thyroid and parathyroid tissue. The animal is then left dependent on the parathyroid graft. By the theory we have now before us we should not expect acute symptoms if the graft "takes," but on its subsequent removal they should develop. The difficulty of making successful grafts is by no means small: Leishner,* for example, in a series of eighty experiments failed over seventy times. The most recent series is that published by Halsted,† of eleven dogs in which he transplanted parathyroid tissue to the sheath of the rectus abdominis, subsequently removing the thyroid glands. His experiments are of interest as marking a new line of investigation. Among his conclusions are the following: First, one parathyroid graft may suffice to maintain the animal in good

* 'Arch. f. klin. Chir.,' 1907, lxxxiv, p. 208.

† 'Journ. Exper. Med.,' 1909, vol. xi, p. 175.

health and spirits for many months, and possibly for years. Second, parathyroid tissue is essential to the life of dogs, as has been conclusively proved by the result of excision of the sole sustaining graft.

On examining his experiments more closely, we find that of the eleven cases, five died with definite pathological lesions, unconnected with the parathyroids, such as pneumonia and peritonitis. In three others the experiments are not yet complete, while in nine out of the eleven cases no histological examination was made to identify the grafts as parathyroids, or to prove the absence of other parathyroids post mortem. The two remaining experiments, however, are better able to support deductions. In the first the graft was removed after twelve days and the dog died three days later. Histologically the graft was partly thyroid and partly parathyroid. In the second, the graft was removed after three and a half months and the dog died two days later. But, as in the preceding case, this graft proved to be made up of thyroid tissue with some smaller areas of parathyroid tissue. In these two cases, though the experiments were more complete, we can hardly say whether death was due to the loss of the thyroid or the parathyroid portion of the grafts.

Leaving now the experimental side of the question, we may seek further support for the theory in the pathology of the glands. From the one side we may hope to identify some train of clinical symptoms with some particular lesion of the parathyroids. From the other side we might examine a large series of glands, and whenever we found a morbid change, analyse the clinical records to discover some features common to all the cases and referable to the lesion.

The first of these lines of inquiry has, up to the present, been barren of results. Naturally enough, many observers have sought a connection between convulsive states, such as tetany and parathyroid disease, but post-mortem and histological proof have not been forthcoming. Harnett,* Humphry,† Thompson‡ and myself§ have examined the glands in cases of tetany and convulsions, but without finding any definite change. Pepere,* however, describes the case of a young man who died on the fourth day of an illness characterised by muscular spasm, opisthotonos and trismus, and diagnosed during life as tetanus. Post mortem the profound visceral congestion that occurs in tetanus was observed as well as subserous ecchymoses, pulmonary hæmorrhage and other changes. The parathyroids were noted as atrophied. As no site of inoculation by the tetanus bacillus could be found, Pepere felt justified in suspecting a parathyroid deficiency as the cause of the symptoms. (It will have been observed, however, that the case as described was in no way suggestive of tetany, but both in its symptoms and course resembled an example of tetanus.) Of other diseases with nervous symptoms which have been claimed as dependent on the parathyroids I may mention eclampsia, epilepsy, paralysis agitans and pellagra.

With regard to morbid histology, we find that though the glands are subject to most of the pathological changes that affect other tissues, they may be diseased without producing clinical effects. Among the morbid changes that have been described are hæmorrhages, congestion, fibrosis, amyloid, hyaline, colloid and cystic degeneration, fatty changes, pigmentation, and so-called new growths. In no case have these changes been known to produce recognisable symptoms.

These facts lend no support to the theory. Indeed, they tend to weaken it, for if the glands are of supreme importance we should expect that when diseased they would produce some disturbance of health. On the whole, we must conclude that neither experimental investigations nor clinical and post-mortem research warrant us in regarding the parathyroids as organs endowed with a special function essential to life.

There is, however, yet another direction from which we might expect evidence in support of the theory. If the glands are physiologically important, the fact is likely to have impressed itself on those surgeons who have the most frequent opportunities of removing the thyroid for goitrous and other conditions. Has their experience taught them the practical necessity of preserving the parathyroids intact? Or do they find that without taking this precaution they do not meet with the symptoms attributed to parathyroid deficiency?

* 'Path. Soc. Trans. Lond.,' 1907, vol. lviii, p. 128.

† 'Lancet,' 1905, vol. ii, p. 1390.

‡ 'Amer. Journ. Med. Sci.,' Phil., 1907, vol. cxxxiv, p. 562.

§ 'Quart. Journ. of Med.,' vol. i, p. 287.

* 'Pathologica Genoa,' i, p. 97.

Observations on this point would be of considerable value, and I hope that Sir Victor Horsley and Mr. Berry will let us hear their opinions.

We now come to the alternative view that the glands are part of the thyroid and possess an identical function.

At the outset we must notice that both in man and mammals the most careful dissection and histological examination of the tissues in the neck have failed, in some cases, to reveal any parathyroid tissue at all. This fact, now attested by numerous observers, is by itself sufficient to cast serious doubt on the importance of the glands, for how can an organ be essential to life if some of us can get on without it.

Further suggestive facts have been brought to light by ascertaining the relation between the parathyroids and accessory thyroids. As a result of examining some sixty human bodies I was able to show that the majority of parathyroids are found in a very narrowly limited area, which happens, likewise, to be the site of the majority of accessory thyroids; also that the number of the parathyroids decreases throughout life from a maximum in infancy, but the number of the accessory thyroids increases from a minimum in infancy. The implication is that the parathyroids undergo gradual conversion into accessory thyroids.

The strongest evidence in favour of the identity of the two glands comes to light when we study their comparative histology. A typical thyroid with vesicles lined by single layers of epithelium and filled with secretion presents a sufficiently characteristic picture. A typical parathyroid composed of massed polyhedral cells, with a few scattered drops of colloid and an occasional primitive vesicle, is also sufficiently characteristic. But between these two extremes we can find every gradation of structure. Beginning at the thyroid end of the series, we shall first notice how little clusters of polyhedral cells get inserted between the vesicles. These I have described in animals as little related to each other as man, a green monkey, a hyæna and an eagle. Next we shall come to thyroids in which these cells form large clumps, and in these clumps we shall observe that the cells are partially rearranged to form minute vesicles. These are filled with little drops of colloid, and their lining cells become pressed into a cubical or columnar shape.

Still further along the series we shall meet with thyroids which consist chiefly, and, in some cases, exclusively of these interstitial cells. Glands of this class have lost all the characteristics which we associate with a normal thyroid, except the power of secreting colloid. They are made up of a solid mass of polyhedral cells. Such organs I have described in a number of animals, such as a weasel a beaver, a piping-crow, a bat, an antelope, a quail, and a falcon. They are, therefore, very widely distributed throughout the animal kingdom.

Now it is quite obvious that when we have reached a thyroid made up of massed polyhedral cells, with a few primitive vesicles and occasional drops of colloid, we have the histological picture of a typical parathyroid. Suppose our section came, not from the thyroid itself, but from a gland in its neighbourhood. How are we to decide whether we have found a parathyroid or an accessory thyroid? Such isolated bodies do occur. I have illustrated one from a four-horned antelope. Another I found in a Malayan bear and a third in a golden agouti. Recently Calderara* has described such a gland in a human subject; he was, he says, unable to decide whether it was altered parathyroid or an accessory thyroid.

If, now, we begin at the parathyroid end of our series we shall find that the typical parathyroid is succeeded by others with numerous vesicles and ample colloid secretion. They now begin to resemble the thyroid, with interstitial cells which are forming small vesicles. Again we shall be unable to decide between the two.

The comparative histology of the glands, then, provides us with striking evidence of the identity of the two structures. We must conclude that the parathyroids are portions of the thyroid which have assumed functional activity without yet taking on the features of the adult gland.

It only remains to mention the changes in the parathyroids when the thyroid itself is diseased. In exophthalmic goitre degenerative changes with overgrowth of connective tissue have been described by Benjamins and MacCallum. In one case examined by myself one of the parathyroids showed an unusual activity of colloid secretion. With regard to myxœdema the parathyroids have been examined in only two cases, in both of which some of the tissue appeared normal, but some

* 'Arch. Ital. de Biol.,' I, fasc. ii, p. 190.

showed definite changes, leading to an appearance suggestive of thyroid tissue. Finally, in three cases of cretinism cystic degeneration of the parathyroids had occurred.

The pathogeny of goitre.—As a result of examining many thyroid and parathyroid glands I gradually became impressed by the mechanical importance of some of their structural features. Later, the connection between these features and certain pathological changes in the thyroid became obvious, and I further attempted to trace their share in the production of enlargements of the gland. I propose very briefly to summarise certain conclusions that have suggested themselves with regard to the pathogeny of goitre.

Considering first the secretion of the parathyroid colloid, we find that the oxyphile granules of the cells are extruded into the intercellular spaces, where they collect, forming minute drops of colloid. As each of these increases in size the surrounding polyhedral cells are forced apart, opening a central space in which the secretion is accommodated. The cells, subjected to the radially exerted pressure of the colloid and to the mutual lateral pressure of the adjoining cells, lose their polyhedral outlines and become cubical or columnar. A lining epithelium is thus made and a vesicle is formed. From the latter the colloid passes into the lymphatic capillaries, thence to the larger lymphatic channels, and finally drains away from the gland. We see, therefore, that the mechanical influence of the colloid is able to convert the closely packed polyhedral cells into definitely formed vesicles.

In the thyroid similar changes occur. They may be watched either in fœtal life or at later ages in any gland that contains areas of the interstitial cells I have already mentioned. The formation of thyroid vesicles from solid masses of thyroid cells is therefore directly dependent on the mechanical pressure exerted by the secretion. But since the interior of the vesicles communicates with no special efferent ducts, the colloid has to find its way as best it can into the lymphatic vessels and thence to the exterior. The mechanical obstacles in its path are great. Not only is it unprovided with special ducts along which to flow, but it is itself peculiarly viscid. These difficulties are further increased by the fact of the considerable size of the thyroid, which is by far the largest gland without a system of ducts. So primitive is its system of drainage that often its colloid is unable to escape from some of the vesicles and becomes pent up, forming a cystic collection.

Next let us imagine some interference with the outflow of colloid, not merely from one or two vesicles, but from the whole organ. We can readily picture the results. The colloid is no longer able to flow through the lymphatics. It is dammed back in the vesicles. The latter are distended and the entire gland becomes uniformly swollen. If the obstruction is made permanent some vesicles are certain, sooner or later, to become more dilated than others, and thus cysts of various sizes will be produced.

Now compare these hypothetical changes with the changes which we know occur when a simple or parenchymatous goitre is being formed. In the earliest stage the thyroid is uniformly enlarged and still retains its normal proportions. On section its vesicles are everywhere distended with colloid. Later some of the vesicles become over-distended and form small cysts. Later still the membranes between adjacent cysts often become absorbed, and in time the parenchymatous goitre becomes a cystic goitre.

With regard to the causation of the various pathological enlargements of the thyroid, attention has been usually directed to the possible alterations, quantitative or qualitative, in the secretory activity of the epithelial cells, but it seems to me that, in ordinary goitre at any rate, we must blame, not the cells for any perverted function, but the efferent channels of the gland which fail to perform their work. In other words, we should regard goitre as the result of a pathological change in the lymphatics of the thyroid rather than of a disturbance of its secretory powers.

We may follow the point a step further. If we accept the view that goitre is an infection by a parasite—and for myself I consider that the evidence points strongly in that direction—then the facts I have mentioned indicate, if they are correct, that the parasite produces its primary effect on the lymphatics of the thyroid, either obstructing them or causing changes which lead to their obstruction. Further, the goitrous enlargement being at first uniform, it is to the main lymphatics of the gland that we should look for the original cause of the goitre.

If these contentions are well founded they imply

that in goitrous subjects the secretion of the thyroid is prevented from entering the circulation through the usual channels. Why, then, it will be asked, are not all goitrous subjects myxœdematous? My reply is that many of them are myxœdematous, and that in the remainder an alternative route is formed by which the colloid finds its way into the circulation. Cretinism, which is juvenile myxœdema, is due to the loss of the thyroid function, yet, strangely enough, the majority of cretins have goitres. This is an extraordinary and perplexing fact, which, so far as I know, has never been explained. The difficulty has been to account for the development of cretinous symptoms in individuals whose thyroids are actually larger than normal, and contain demonstrable glandular tissue with a secretion of colloid often copious enough to form cystic collections. Yet by assuming that the efferent channels from the gland are completely obstructed we can readily understand how even a large goitre may co-exist with cretinism.

In adults, however, a goitre producing myxœdema is rare, although, nevertheless, the association has been observed. But in the majority of cases no myxœdematous symptoms arise. I interpret this as showing that the colloid, finding its natural outlet barred, seeks and finds another channel of escape. But if we exclude the lymphatics, there is only one other possible route open to it, namely, by the blood-vessels. This I believe is the route taken, and by this fact we are able to account for the absence of myxœdematous symptoms. This explanation is not merely theoretical, for I am able to support it with experimental proof.

Since King, a surgeon at Guy's a century ago, showed by direct experiment that colloid passed into the lymphatics, many observers have described it as of normal occurrence in the lymphatics of the healthy thyroid, and Sir Victor Horsley has found it in adjoining lymph-nodes. Both these occurrences I have myself observed. In connection with observations on goitre, however, I have found but three papers dealing with the lymphatics and blood-vessels of the thyroid in this condition. Podbelsky,* in 1892, examined the lymphatics in twenty human goitres and found that in no less than fifteen—75 per cent.—they contained no colloid. In the following year Horne,† working under the direction of v. Recklinghausen, described a similar condition in fourteen out of his eighteen cases—78 per cent. These observations go to show that in goitre colloid does not escape by way of the lymphatics.

Previous to these investigations Gutknecht,* in 1885, had made a discovery that many of the blood-vessels in goitrous thyroids contained colloid. Horne confirmed this observation, finding, in addition, that the secretion lay only in the veins and not in the arteries. Although none of these workers appreciated the bearing of their observations on the pathogeny of goitre, their results, taken together, provide the experimental proof of the explanation I have given.

I conclude, therefore, that goitres are produced by the obstruction of the lymphatic vessels of the thyroid, and that in many cases the colloid escapes by the blood-stream. In other cases, however, no alternative outlet is found, and in them the symptoms of myxœdema inevitably follow.

(To be continued.)

July 26th, 1909.

* 'Med. Woch.,' Prague, 1892, xvii, pp. 197 and 211.

† 'Journ. Anat. and Physiol.,' 1893, xxvii, p. 161.

* 'Virch. Arch.,' 1885, Bd. 99, p. 314.

The Differential Diagnosis of the Acute Exanthemata.—In measles the most valuable indication is the Koplik spots. These appear sometimes on the first day of the prodromal fever, and are distinctly evident by the second day. They last from four to six days. Scarlet fever is often mistaken for diphtheria. The points of differentiation are that the mucous membrane around the angina is redder than in diphtheria, the lymph glands more swollen, the pulse higher, and the odour of the breath sweetish, while in diphtheria it is foul. Variola is suggested by the severe headache and backache. The prodromal rash may be mistaken for measles or scarlet fever. The lack of Koplik spots and the freedom of the face from rash point to the correct diagnosis. In adults the first rash of measles may be papular and suggest smallpox. "Stomach rashes" in infants may resemble measles, but lack the prodromal and the Koplik spots renders the diagnosis possible. Drug rashes, resembling measles, can be told by the greater itching and occasional urticarial patches. German measles is characterised by absence of prodromals, the slighter rash, more ephemeral temperature, and shorter duration. *Medical Record*, vol. lxxvi, No. 2.

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* *Specially reported for the Clinical Journal. Revised by the Author.*

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A CLINICAL LECTURE

ON

RHEUMATOID ARTHRITIS.

Delivered at St. Bartholomew's Hospital.

By W. P. HERRINGHAM, M.D., F.R.C.P.,
Physician to the Hospital.

GENTLEMEN,—I want you to look at the joints of this patient, a middle-aged woman. The chief thing left at present is a thickening of the metacarpo-phalangeal joints, but there was at first considerable swelling about the elbows. There is a little fulness in the left one still, and when she came to us the other day she had a decided thickening of the periosteum of the olecranon, and it was very tender and red. She had the same sort of condition on the knuckle, which is still slightly deformed. She has also had swelling in the ankles, which prevented her standing properly They are now much better. There has been considerable pain, but her heart is perfectly natural. She was admitted on May 29th, and her story was that the pain came on suddenly on May 26th in these various joints, and that she had an attack of what she calls "rheumatic fever" in 1906. She was then ill for four months, and she has had attacks in her joints twice a year since, always in her hands and feet. Her heart remained perfectly natural, and the length of time which the first onset took—four months—and the repeated attacks of rheumatism or arthritis in the joints without any lesion of the heart, together with the characteristics of those joints themselves, led me to believe that she had not any ordinary rheumatism, but arthritis from some other cause. We could not get evidence of any other cause. But there was one symptom which I always believe to be characteristic of arthritis due to the gonococcus, and that was great pain at the back of the heel.

As far as I know, pain there, which I believe is in the attachment of the tendo Achillis, is invariably gouty or gonorrhœal. And putting that together with the chronic condition of her lesions and the absence of heart disease, I believed it to be a case of gonorrhœal rheumatism, and on that account I gave her a vaccination with the gonococcus. On the first occasion we gave 25 million and on the 19th of this month 15 million gonococci. Although that treatment has only been employed twice up to the present, she reports that she is without doubt considerably better.

We have another man now in the wards in whom the same treatment has been employed. He had a definite gonorrhœa at the time. There was no visible discharge in the woman, nor was the gonococcus found in the vagina. But it has to be remembered that gonorrhœal rheumatism is not necessarily a lesion of acute gonorrhœa; it may come on years after the original gonorrhœa, when there may be no trace of any gonorrhœal discharge at all, either gleet or purulent discharge.

Now I want to show you another case, which is of a completely different character, namely, hæmophilic arthritis, in which the lesions are mechanical in origin. Look at this elbow. (The elbow was greatly enlarged and deformed, and movement much impaired.) He has also lesions in the knees, in the right knee especially, with extreme grating in the joints. We know that he is a bleeder, and these lesions are very common in hæmophilia. Originally they are caused by hæmorrhage into the joints, and this goes on to produce organic changes in the tissues of the joints themselves. First of all there is a deformity produced by the sanguineous effusion, and then changes go on, and produce a condition which it is difficult to distinguish from the ordinary lesion of osteo-arthritis—that is to say, an increase of bone, hardening of bone, erosion of cartilages, and eventually organic adhesions. I show you specimens from the Museum of the sort of condition which this boy has in his knee. His knee feels exactly like a typical case of osteo-arthritis in an elderly person.

Here is another boy, æt. 15 years, who has been under my care for a different disease some two or three times before this. The first time, I think, was three years ago. I have had him under my observation for at least three years, and he came then with lesions in his knees, which are very much like those which he has now. The right was always the worst knee. It was a soft swelling but not very painful or tender, and there was evidently a considerable amount of effusion inside the joint. The knee-cap could be depressed on pressure. It always prevented movement a great deal, and it was soft and never hot nor red. It looked so exactly as if there must be an enlargement of the bones that we had it skiagraphed. But the skiagram does not show any change in the bones whatever; they are not even rarified, but are perfectly natural. A case like that may go on for a long time. He got very much better the last time he was here. He had a very slightly enlarged spleen then, but no enlarged glands. He looked very pale, as he does now, but the blood when examined did not then show any great anæmia. His other joints affected were, first the wrists, and these joints on the fingers. The elbows he has never been able to straighten since I have known him. At present the loss of extension is very much greater than it has been before, and there is less pronation and supination. There is a little grating in the wrist, and you often find it in these joints without any lesion of the cartilage at all. He has had pain and swelling in the joints of his jaws and neck. As to his other organs, he has a perfectly natural heart. Next, he has a liver which is very large and reaches to the level of the navel. The spleen is also enlarged, and he has enlarged glands in both axillæ, and he has a considerable amount of albuminuria with casts. At present he shows anæmic changes in the blood. The blood-count is three to four million reds, and the hæmoglobin count 50 per cent., colour index ·7, and the leucocyte count 11,200, of which there are 32 per cent. lymphocytes and for the rest no great change. That is a case of rheumatoid arthritis of the young, which is now very often connected with the name of Dr. Still, who described a number of cases which occurred in Great Ormond Street Children's Hospital. The characteristic of that disease, as you see it in the young, is the great distortion and crippling which it produces in the joints. Sometimes the distortion and crippling are extremely rapid in onset. The wasting of muscles which you see very plainly marked in that boy is very characteristic, and is sometimes extra-

ordinary, while the joints may be very little affected. But, as a general rule, the wasting goes with the lesion of the joints, both together producing deformities and crippling, which are very severe in character, generally prevent walking, and often such patients cannot feed themselves. You will find that the joints which are chiefly affected are the knuckles, the first phalangeal joints, the wrists and elbows, and the knees. This boy is an exception rather, in that his finger-joints, now, at any rate, do not show very much change. He has, however, had swelling in his finger-joints in past times. At present there is not so much in the wrists and fingers as in the elbows and knees. Another characteristic of that disease is, that it is very chronic. This patient has been like that, to my knowledge, for three years, and probably it has existed longer than that. Yet it is not always chronic. In a case which I saw from the beginning to the end the disease began as acutely as if it was rheumatic fever, and there were then erythematous rashes with swelling in the joints, going from one to the other, very much like rheumatic fever. In fact I had no doubt about the nature of the disease for many weeks and I was looking for evidence of a lesion in the heart, and wondering why under the repeated doses of salicylate of soda the pain was only relieved for a time, and came back again. I could not understand how it was I could not cure the disease. That went on and the fever went on, off and on in periodic attacks for a period of two or three months, and it was not until after that time that the characteristic deformities of the wrists began to manifest themselves, and then we were obliged to confess it was a case of rheumatoid arthritis. But I can assure you that at first it was indistinguishable from a case of ordinary rheumatic fever. When you see cases in the condition of the patient before you they are easily distinguished, but not at first. Another characteristic of it is that the heart is hardly ever affected. I have never seen the heart affected at all, but I believe it has been known to be affected in rare cases. As the disease goes on you see what happens. The joints, which were at first temporarily swollen and painful, gradually became continuously swollen so that great deformity exists, and yet you would be surprised if you could see how those cases can be improved under hot-water douches at Aix-les-Bains, in the South of France. I have seen a joint as bad as that in the knee and elbow become perfectly flexible, so that the child could move the knee and elbow freely and without pain, and the shape almost returned to the normal, but not quite. Then as the disease goes on the joint becomes the subject of organic changes. This sort of soft swelling in the parts which you see here is due to hypertrophy in the villi of the synovial membrane and to gelatinous increase in the synovial fluid. It gradually passes into a condition of fibrous ankylosis, the fibrous strands running between the two surfaces of the joint and on the outside of the joint until the whole is tied up by adhesions which are past recovery. Eventually those adhesions ossify; there may be regular osteophytes in some parts of the joints, yet they are not quite like the osteophytes of senile osteo-arthritis, and they never get the eburnation which is common in that. They are spicular, or there are strands of cancellous tissue running up the fibrous adhesions. When you get that condition the joints are deformed and immovable beyond recovery. Further changes you may find in the glands, which are often, in fact, I think usually, enlarged in these cases. Enlargement of the spleen also often takes place, but not always. This boy has that enlargement very well marked, and in the other case I have spoken about it was also very well marked. I have never before seen a case of enlargement of the liver in this disease such as this boy shows, and what that enlargement is due to I do not know. It has come on since he was here last, so that it is probably connected with the rheumatoid arthritis. It may possibly be amyloid. He has albuminuria and casts which might possibly also be due to amyloid, but so far as the cases have been examined post-mortem, those symptoms are due to nephritis and not to amyloid disease. They end, like ordinary nephritis, in uræmia and death. I have seen it end so.

A case like that you have to distinguish, in the first place, from rheumatic fever, but that difficulty only occurs in the onset, when it is acute. The next thing that some people distinguish it from is a very similar condition in older people. You often find rheumatoid arthritis in young or middle-aged women, up to forty years of age, and I myself believe that that is the same disease as occurs in these children. I think that the more frequent

enlargement of glands and enlargement of spleen in children is probably only due to the more easily reacting tissues of the child, and perhaps to the more virulent poison, which can grow more satisfactorily in the child's tissues than in the young woman's. The disease in young women is a longer lasting one, and not nearly so fatal as those cases in the child. Otherwise I believe it to be the same disease. These cases in women are often connected with some uterine irritations. It need not be gonorrhœa. They have been shown to be often coincident with some uterine irritation, and if the uterine irritation is improved the disease is apt to improve too. Dr. Cave, of Bath, called attention to this matter some years ago. You have also to distinguish it, though it is not difficult to do so, from the cases of true eburnating osteo-arthritis in the old. That I think is so distinct a disease, and so well recognised as a separate disease, that I need not enlarge upon it. The first thing to consider is what is going to be the upshot? In this boy who was before you the result will be death. These cases are seldom recoverable in young children. In a few cases they do recover. In a few you can stop the disease; it appears to go to a certain stage, and then stop. But when once it has got to the stage of nephritis they never recover. The disease lasts for a variable number of years. This boy I think will die within five years from the day of the onset. In some cases the onset is more rapid and in others less so. But the prognosis, although bad, is not always hopeless. So you can always tell the parents of a child like this that although it looks very bad, there is the chance that the disease may stop and the child may recover. Hope is a great help. When the disease occurs in young women the prognosis is very much better. The treatment of these cases is almost exactly opposite to the treatment of ordinary rheumatic fever. These cases want feeding up and nourishing and strengthening in every possible way. For the acute attack I find that salicylate of soda relieves pain and stops the fever, very much the same as in rheumatic fever, but only temporarily. It does not prevent the recurrence of the fever, and these cases are sometimes marked by a periodic fever, very much the same as you get in lymphadenoma, for instance. There is perhaps a fortnight's fever and then a period of apyrexia. I showed you the chart of this case which I got three years ago, and if you were to see the chart of the whole three years you would probably see about a fortnight's pyrexia and then a fortnight's calm, and then a fortnight's fever again. That is very common in these cases. The drugs commonly used and the best ones are iron, iodide, arsenic and cod-liver oil. The best way of giving iron is as iodised syrup of iron, and you can give a minim or two of liquor arsenicalis with it. Cod-liver oil you can give in the ordinary way. Feed these patients up on everything you can—milk, eggs, meat, wine even; cram in as much nourishing food as you can. I think the most important things are baths on the one hand and climate on the other. In the case which I spoke to you about there was no doubt at all of the benefit that the child derived from the baths at Aix-les-Bains in the South of France. I do not think the baths of Bath have so good an effect. I have never seen a case which benefited so much as the one I have in my mind, and perhaps cases differ in the influence which baths may have upon them. But there was no doubt at all about the improvement in that instance under hot douches at Aix, the waters of which contain sulphur and iodides chiefly. And also there was no doubt about the improving effect of a hot, dry climate. Two climates were tried for that case, Egypt and the Canary Islands, of which certainly the Canary Islands was much superior. The case was treated in Las Palmas, Grand Canary. The previous winter was spent by the patient at Helouan, near Cairo, with very little benefit. But it is only right to add that it is possible the disease was already slowly wearing itself out by the time the child went to Las Palmas. At the end of the winter there, though the joints were still deformed, the patient could ride about on a donkey and enjoy life, but he had nephritis and uræmia, of which he died.

August 2nd, 1909.

Two Hamburg physicians have found that in manic depressive insanity and dementia præcox a small amount of some material circulates in the blood, the presence of which may be proved by a biological reaction. The reaction also appears in patients who show no sign of cyclic insanity, but in whose family it has occurred. The reaction consists in the blood of such patients preventing the hæmolytic action of cobra venom on normal blood.—*Medical Record*, vol. lxxvi, No. 3.

A CLINICAL LECTURE

ON

POPLITEAL ANEURYSM.*

By HUGH M. RIGBY, M.S.Lond., F.R.C.S.Eng.,
Assistant Surgeon to the London Hospital.

GENTLEMEN,—Aneurysm occurring in the vessels of the lower limb is most frequently found in the popliteal artery. During the last fifteen years twenty-eight cases of aneurysm of the vessels of the leg have been admitted into this hospital, and of these twenty were situated in the poplitéal space. The treatment of this condition has always been a matter of great interest. Time-honoured methods such as compression or ligature of the main vessel leading to the aneurysm are probably familiar to you. My reasons for giving this lecture are: (1) To remind you of a comparatively new operation devised for the treatment of this condition; (2) to illustrate the same by two cases which have recently been under my care in the hospital; (3) to inquire into the advantages of this operation, and to form an opinion (if this be possible on such scanty material) as to whether its adoption is justified by the results obtained.

The operation I allude to is termed "arteriorrhaphy" or "endo-aneurysmorrhaphy," and was first introduced to the notice of the surgical profession in 1902 by Rudolph Matas, a surgeon practising in New Orleans. His first experience of this treatment was in the case of a negro as long ago as 1888. This man had an aneurysm of the brachial artery which was steadily increasing in size. Matas first ligatured the feeding vessel on the proximal side of the aneurysm, but owing to an extensive collateral anastomosis this treatment proved unsuccessful, and pulsation returned in the sac. At a second operation an attempt was made to dissect out the sac of the aneurysm; he found, however, that the median and ulnar nerves were so intimately adherent to the vessel wall that removal of the aneurysm would have meant inevitable division of these structures. He then conceived the idea of opening the aneurysm and attempting to close the feeding vessels from within the sac. The openings of the main vessels were closed by rows of sutures passed through the intima, and a similar treatment was carried out in the case of some large collateral branches which were found to open into the sac wall. The result was most gratifying. The intima was found to hold the sutures perfectly. No hæmorrhage followed and the patient was completely cured. Up to the present time, namely, twenty years afterwards, no recurrence has taken place. Encouraged by this success he tried a similar operation in other cases, until in 1902 he was able to publish five cases treated in this way and to formulate his views of the procedure. His example was followed by other members of the profession, chiefly in his own country, so that three years later, in 1905, twenty-four similar operations were reported from various sources. Next year the number had risen to thirty-four, and in June of last year, 1908, no less than eighty-five cases were collected in which this operation had been performed. These included aneurysms of various arteries, and illustrated the results obtained by the various modifications evolved from the original operation. These I will allude to presently.

It appears (from these eighty-five published cases) that this method has not been given much of a trial in this country; out of the eighty-five cases only one came from an English clinic, namely, Birmingham. It may be that cases have not been published or that surgeons in England are satisfied with the results obtained by older methods, or that, as is usual, a new line of treatment is looked upon with a certain amount of criticism. It will, I think, be worth while at any rate to consider (1) the rationale of this new line of treatment; (2) the reported results of cases published up to date; and then compare with these (as far as one can) the results obtained by the more familiar methods of treatment.

Let me shortly describe the usual pathological conditions found in a case of aneurysm of a vessel of the limb, and remind you that I deal to-day with aneurysm dependent for its existence on the usual combination of causes, namely, disease of the vessel wall due most frequently to syphilis often combined with a localised injury or strain to the affected part. I exclude all those cases of acute aneurysm, either multiple or single, secondary to active disease of the heart or its valves.

In a simple case of aneurysm the conditions found may be as follows:

* Delivered at the London Hospital.

(1) True sacciform or sacculated aneurysm. In this form an opening in the vessel wall leads into the sac of the aneurysm. The opening only involves a portion of the circumference of the vessel wall. The lumen of the vessel is not altered and the blood-current not arrested; the circulation below is good. Pulsation may be felt unaltered or perhaps slightly delayed in the distal parts of the limb.

(2) The more common condition (at any rate in aneurysms of the popliteal artery). The opening in this case has either increased, or so much of the circumference of the wall of the vessel has been involved, that a more or less fusiform condition has resulted. The sac in the case of aneurysm of the popliteal artery is usually formed of most of the circumference of the wall of the vessel, the exception being that part directly in contact with the bone and posterior ligament of the knee-joint.

In this form two arterial openings are found on opening the sac, generally one and a half to two inches apart, and the sac wall is much thinned out and often extends in pouch-like recesses beneath the surrounding muscles and soft parts. The wall of the aneurysm in its peripheral parts is much altered. It presses upon the surrounding veins, arteries, and nerves, and becomes closely adherent to them. It has a false outer wall formed by sclerosis of the surrounding tissues. In addition, large vessels, increased in size owing to the need for collateral circulation, *may* be seen entering the sac wall in various places. According to Matas's experience 66 per cent. of all popliteal aneurysms are of this character.

Now let us consider the methods of treatment generally adopted. (1) *Compression.* In pre-operative days, and, indeed, up to comparatively recent times, treatment consisted in attempts made to shut off the circulation through the aneurysm and so induce gradual clotting of the blood in the sac. This was carried out either by direct pressure to the tumour itself or more commonly by compression of the main vessel on the proximal side. I well recollect in the days of digital compression how I and several other members of the football team were pressed into the service, and spent long hours exerting violent pressure on the femoral artery of an unfortunate patient the subject of a popliteal aneurysm. I often wondered who suffered most, the patient (who really suffered a great deal and had to be kept under morphia) or the handy men who were enticed into the entertainment. The results at any rate (if one only knew it at the time) were certainly not always commensurate with the amount of energy expended. No doubt a certain number of cases were successful, and there is a good specimen in our museum showing an aneurysm filled with clot and cured by this treatment.

(2) Hunter's operation of ligature of the vessel at some distance from the aneurysm is the method commonly used even now.

(3) *Anel's method*, or ligature of the feeding vessel close to the sac, has been of late years revived, as the fear of disease of the vessel wall near the sac was discovered to be without foundation.

(4) *Extirpation of sac.*—This is a comparatively modern method of treatment. The sac is either excised after the feeding vessels above and below have been ligatured, or the feeding vessels are tied off and the sac opened and drained, the walls being allowed to close gradually by granulation tissue.

Now I want to briefly outline the method adopted by Matas, which essentially consists of direct suture applied to the intima of the vessel wall. The procedure is carried out with three different points in view:

(1) In the case of true sacciform aneurysms to simply close the small opening leading from the lumen of the vessel into the sac of the aneurysm. This is effected by sutures passed laterally on the Lembert principle. The sac is then obliterated by several sutures. This operation is entitled *restorative endo-aneurysmorrhaphy*. It is the ideal operation, and affects in no way the circulation of the limb below the aneurysm.

(2) In the case of aneurysm of the fusiform type (and this is generally found in the cases of popliteal aneurysm) two distinct methods are possible: (*a*) The openings leading into the sac are obliterated by sutures passed from within on the Lembert principle, through the intima of the vessel wall. The cavity of the sac itself is then obliterated either by rows of sutures or by inversion of the overlying soft parts. This is called *obliterative endo-aneurysmorrhaphy*. (*b*) An attempt may be made in this type of aneurysm to restore the vessel wall by suturing the lateral walls of the sac over some form of tube.

removed before the last suture is finally tied. This is called reconstructive endo-aneurysmorrhaphy.

The ideal operation is, of course, restorative endo-aneurysmorrhaphy, but unfortunately, in aneurysms of the popliteal artery its employment is very rarely possible owing to the infrequent occurrence of a true "sacculated" aneurysm. Reconstructive endo-aneurysmorrhaphy will probably be seldom performed; so that in the average case of popliteal aneurysm the method of obliterative endo-aneurysmorrhaphy is the operation which we may with benefit consider to-day. From a practical point of view it will be best to discuss the superior advantages of this method over—(1) ligature of the feeding vessel; (2) extirpation of the sac. The points in its favour are: (1) It is proved without doubt that the arterial openings into the sac can be securely closed by suture. That all openings, not only those of the main vessels but of collaterals, can be directly dealt with. (2) The contents of the sac are emptied out and therefore pressure on the surrounding structures, especially the vessels, is immediately relieved. The return of venous blood and the circulation in the collateral vessels is restored. (3) The sac can be obliterated and made use of to strengthen the tiers of sutures which close the arterial openings.

Now let us inquire into the reported results of this operation. In June, 1908, eighty-five cases were published; fifty of these were aneurysms of the popliteal artery. In thirty-two cases the above operation, namely obliterative endo-aneurysmorrhaphy, was performed, in eight cases the restorative operation, in ten cases the reconstructive. Results in the popliteal aneurysm cases: One death from tetanus. Two cases of gangrene (but in one of these the vein was ligatured also). There were three relapses (all these occurred in the reconstructive operations). In one case secondary hæmorrhage occurred, and this led to subsequent amputation of the leg. There was only one case of gangrene really secondary to the intra-saccular operation.

In the obliterative operations there were no relapses, no case of secondary hæmorrhage, and sound cures were obtained in all the other cases.

In order to get some idea of the value of these figures I have compared them with the results of ligature and other methods of treatment adopted in this hospital during the last fifteen years. I find there are altogether twenty cases of popliteal aneurysm in the case-books. They occur generally in young men, the average age being about thirty-five. They nearly all gave a history of syphilis, and very often an additional history of an injury to the affected part. In the last fifteen years, twenty cases of popliteal aneurysm. Results: Nine cases were treated by ligature of the artery in Hunter's canal. In one case pulsation returned in the sac and the sac was excised at a second operation with good result. In three cases gangrene followed $=33\frac{1}{3}$ per cent. Two of these three cases required amputation of thigh. In the other case the gangrene was limited to the toes, which gradually separated. Three cases were treated by ligature of the artery in Scarpa's triangle; the results were good. Three cases were treated by ligature of the first part of the popliteal artery. Result: One case of gangrene of the toes followed $=33\frac{1}{3}$ per cent. One case was treated by ligaturing the artery above and below the sac, with opening of the sac and turning out the clot. Result: Secondary hæmorrhage occurred, and at a second operation a vessel opening into the sac was found bleeding and was ligatured; the case recovered. One case was not operated on. Of two cases of ruptured aneurysms, in one the sac was excised. Result: Died three days later of uræmia. In the other amputation of the leg was performed; the patient died twenty minutes later. In one case the sac was opened; the vessels were ligatured and the bleeding points secured. The case ended in recovery.

The treatment by excision of the sac must always be very difficult, and carries with it the risk of injury to the surrounding parts, nerves, veins, and vessels. The wall of the sac is often pouched and adherent to surrounding structures, rendering its removal a matter of much tedious dissection.

There can be no doubt on consideration of these results (which, to say the least, are somewhat startling) that there is some good reason to consider most carefully the new treatment which I have reminded you of to-day. The probability is that many English surgeons are employing this method now, and no doubt in time results will be published which may or may not confirm those already obtained in other countries.

My experience of the operation is that it is not difficult but tedious; the obliteration of the sac wall is not easy, and the length of time taken over the operation, with a tourniquet applied to the limb, might have grave disadvantages.

I should like in conclusion to read brief notes of two cases which I have operated on by the obliterative method, and to show them to you. One of them has only recently left the hospital, the other ten months ago.

The first case was a man, æt. 60, who for three months had had aching pain in the left leg and knee. One month before admission to the London Hospital he noticed a slight swelling behind the knee; this had gradually increased in size. The leg swelled when he walked. His condition on admission was noted as follows: "There is a well-defined pulsating tumour in the left popliteal space. It is tender on pressure and has an expansile impulse and systolic bruit. The apex of the tumour is close to the skin and feels thin-walled. Pulsation can be felt in the arteries of the foot. The pulse in the dorsalis pedis is somewhat slowed on the left side. There is no œdema of the foot now. The patient denies syphilis, but gives a history of alcohol. He is a labourer."

Owing to the rapid increase in the swelling and its close proximity to the skin an operation was considered to be urgently necessary. The sac of the aneurysm was laid open and the arterial opening closed by suture after the Matas method. Two main openings were found entering the sac at the upper and lower part of its floor; these were about 1½ in. apart. Between the openings the aneurysmal wall was convex; the dorsal wall of the sac was thinned and its inner lining roughened, but the floor and margins of the arterial openings showed no signs of atheroma. Continuous chromic gut sutures were used to close the openings of the main vessels. The upper opening was closed first; the suture was then continued down across the intervening space and then the lower arterial orifice secured. A second continuous chromic gut suture was superimposed to reinforce the first row of sutures and to partially obliterate the cavity of the aneurysm. An attempt was next made to fix down the skin and subcutaneous structures to the remaining portion of the inner wall of the sac, but this was found an impossibility owing to the pleating and irregularities of the sac wall. The rest of the sac was therefore obliterated by sutures of chromic gut. The skin wound was finally closed, a small drainage-tube being fixed in at its lower end. The patient made a good recovery. Very slight pulsation could be felt in the posterior tibial artery thirteen days after the operation. The condition now is perfect. No trace of the aneurysm can be felt. The leg is warm and no œdema is present. The patient does hard work.

The second case was that of a man, æt. 32 years, who had noticed aching and stiffness of the right knee for about a month. He worked at heavy labour in a brewery, but had not been able to work for a week before admission into the London Hospital. He had been a soldier and had had syphilis. There was a large expansile tumour situated in the right popliteal space 4½ in. in length and 6 in. transversely. It had an expansile impulse checked by pressure on the vessel above; there was a harsh systolic bruit heard on auscultation. The anterior and posterior tibial arteries could be felt to pulsate well. The leg below was swollen and somewhat œdematous. In this case the Matas obliterative operation was done. An Esmarch's bandage was applied, and after elevation of the limb a tourniquet was fixed round the thigh. A 4 in. vertical incision was made over the aneurysm. The external saphenous vein and popliteal vein were first met and displaced to one side. The sac was found to extend beneath the calf muscles; these were retracted. An incision was made into the sac and the contained clot turned out. There was a thick layer of laminated clot adherent to its inner wall; this was removed by gauze swabs and forceps. The aneurysm was fusiform in type; one fairly extensive pouch lay on the outer side beneath the outer head of the gastrocnemius. The two openings of the main vessel were found about two inches apart. There were no collateral vessels seen in the sac wall. The margins of the arterial openings appeared healthy as did the intervening portion of the sac wall; the parietes of the aneurysm were, however, much thinned and the wall friable. The arterial openings were sutured and the floor of the aneurysm also. Two layers of superimposed chromic catgut sutures were inserted on the Lembert principle The rest of the cavity of the sac was gradually obliterated by chromic gut sutures, the skin wound sutured with silk-worm gut. A small drain was left in. Recovery was complete. The foot remained warm and no signs of gangrene were seen. Pulsation could be felt in the dorsalis pedis artery when the patient left hospital. There is now no swelling of the leg; the circulation appears good. The scar is firm and there is no trace of the aneurysm to be felt. Slight pulsation can be felt in the dorsal artery of the foot but not in the posterior tibial artery.

August 2nd, 1909.

DISEASES OF THE THYROID GLAND.

A Debate held under the auspices of the Hunterian Society.

Dr. ARTHUR T. DAVIES, President, in the Chair.

(*Continued from page* 256.)

THE PRESIDENT, referring to the opening meeting a week before, said that on that occasion the medical aspect had been particularly dwelt on, and at the present meeting the surgical point of view would be discussed. Sir Victor Horsley had been kind enough to attend to introduce that side of the question, and he would be followed by Mr. James Berry. Afterwards the discussion would be thrown open to Fellows of the Society or those who were attending as the Society's guests.

Sir VICTOR HORSLEY, F.R.S., said: Mr. President and Gentlemen,—I thank the Society very much, and yourself in particular, sir, as your interest in the subject of internal secretions is well known, for the opportunity you have afforded me of taking part in this discussion. I ought to apologise to the meeting in one sense, because what I have to say to-night is only founded on my clinical experience; I have no further original work to lay before the Society. It struck me the other night, when listening to the discussion from the medical point of view, that we still require to define what it is we are going to talk about; that there is a need for discussing what exophthalmic goitre really is —we require a clinical definition of it. However, without arguing that point, I can pass on to consider the question now as far as we are interested in it as surgeons, in view of the fact that what we are called upon to deal with is an aberrant secretion of the thyroid gland. If you take a section of a normal thyroid gland, you will find that in practically every single acinus there is colloid secretion, whereas in true exophthalmic goitre there is none. But I have had referred to me, and so must other surgeons interested in the subject, numerous cases of parenchymatous goitre with toxæmic symptoms as exophthalmic goitres. These form a definite class, in which practically the whole gland is enlarged, but the enlargement is always greater on one side than it is on the other. The symptoms are sometimes extremely severe—tachycardia, exophthalmos, a myxœdematous state of the tissues, etc.—and these cases are, I say, constantly described as cases of exophthalmic goitre. But they are not so at all. They are cases of ordinary parenchymatous change such as you see in this slide, with only commencing alteration in the colloidal material, that material becoming of a more liquid character. In them the toxæmic symptoms entirely disappear after a very free removal of two thirds of the gland, while the rest of the gland which is left behind shrinks, and the constitutional disturbance subsides. This excellent result is always to be obtained, in my opinion, in this class of parenchymatous goitre with toxæmic symptoms. I drew attention to this kind of thyroid disease seven years ago at the Chelsea Clinical Society, but for some reason they are still regarded at the present time as cases of exophthalmic goitre. Now we can learn two things from this class of case: first, that the removal of the main mass of toxic secreting gland undoubtedly, as Mr. Walter Edmunds said the other night, brings about great relief to the patient. That is one factor as the result of operation. And the other is, that the operation initiates shrinkage, a beneficent shrinkage of that part of the gland which is left behind. And I think we are indebted to Dr. Forsyth the other night for a very ingenious and ready explanation of how that is brought about, namely, the release of the lymphatic stagnation. However that may be, the consideration of those two points, the removal of the main mass of the toxically secreting gland and the initiation of shrinkage, brings us to the main question of the discussion of exophthalmic goitre properly so-called. If I use the expression "properly so-called," it is because I refer to the condition which you see on the screen—which of course is spoken of now generally as hyperplasia, although I am not sure in my own mind that it is a good phrase—in which the acini are converted into irregular cavities, none of which contain colloidal material, but a precipitate such as you see here, or the contents are wholly liquid, and consequently do not appear in the section at all. This very severe condition, which sometimes terminates fatally, is the "exophthalmic goitre," about which I wish to speak to-night. The essential feature of the case, as it is referred to the surgeon, is this

very profound alteration in the secretion of the gland. But I suggest that on this most important question our clinical observation is very lacking. I look upon this condition of affairs as really the second stage of exophthalmic goitre. Obviously there must be a first stage, because whereas the parenchymatous goitres with toxæmic symptoms begin with a goitre and gradually develop the symptoms, the true exophthalmic goitre begins with the symptoms and later develops the goitre.

Referring a little time ago to your Hunterian Oration, sir, I found you pressed this point very definitely, and yet it is a point which seems to have been lost sight of considerably in the discussion of this matter from the surgical point of view. For it is quite clear that if true exophthalmic goitre can be unilateral in origin, as it not infrequently is, and that if at this early stage it can be entirely and readily cured by the prolonged action of the faradic current together with Weir-Mitchell treatment, as I have seen on more than one occasion, then that cannot be a condition which is wholly due to disordered secretion ; there is something else to which the disorder of secretion is due, and therefore primarily I suggest that we have to make up our minds as to what period of exophthalmic goitre are we going to apply surgical treatment. Is it to be during this first prodromal stage, or during the stage at which the extreme alteration of the gland has been arrived at?

No surgeon, practically, sees a case in the first stage, and therefore we will discuss the cases which come to the surgeon in the second stage. I think Mr. Berry will bear me out that they often come in what might be called the fourth, fifth, or sixth stage, or any stage you like, but a good deal later than the beginning of the second stage. The problem then is, what are we going to effect for the patient by surgical treatment of the gland which is in an advanced condition? I suggest that here, again, we come back to the two points, removal of the toxically secreting gland on the one hand, and the initiation of shrinkage of the remainder of the gland on the other. Professor Kocher, of course, pointed out in his luminous address to the Medical Society that there were two technical procedures to accomplish these objects, and I suppose most of us have had opportunities of carrying them out: first, ligature of the arteries to the gland, and the second the excision of either the isthmus alone or of the lateral lobe alone, or excision of the lateral lobe plus the isthmus. With regard to ligature of the arteries I have resorted to that very rarely, consequently, perhaps, I have no right to criticise the procedure very unfavourably. I would only say my experience has been that it does not afford the same good results as excision, and that therefore I have only resorted to it in cases where I thought the condition of the patient was rather critical for excision. The very last case I had was an extremely severe case which Sir William Gowers referred to me at Queen Square Hospital, and I am bound to say that ligature of all the arteries to both lateral lobes was followed by very great improvement in that case. Still, undoubtedly, on surveying the cases on the whole ligature of the arteries does not produce the same results as those which have been treated by excision.

Then we come to excision. This second procedure of excision is the one upon which we ought to concentrate our attention and make up our minds as to which of these operations should be performed. With regard to excision of the isthmus alone, you know that was first suggested in this country by Mr. Sydney Jones, and in the first case of exophthalmic goitre on which I tried it it was followed by a rapid and permanent cure. I therefore naturally was inclined to go on excising the isthmus, and I have done so in a number of cases, but I am certain that it does not afford the same good results as excision of the lateral lobe. However, I would say this, of course, that the amount of the gland that we take away at an operation must vary with the case, *i. e.* according to the severity of the symptoms, and so for a mild case excision of the isthmus, which is a very trivial operation, would probably suffice. Then we come to excision of the lateral lobe. Curiously enough, it is about this also relatively very simple operation that the discussion of the surgical treatment of exophthalmic goitre has chiefly turned, because when it was first proposed, Brissaud published a series of fatal cases, and in that way the operation was brought into disrepute. As far as I am personally concerned, the first case I operated upon in this manner was a case at University College Hospital, one of most advanced disease, and one on which I should not dream of operating now. That case died. It is obvious that from the point of view of removing a great deal of the toxic gland,

excision of the lateral lobe is the proper course to pursue, and I shall be interested to hear whether it is the experience of other surgeons also that that affords the best result. I think it must be very rarely necessary to remove the lateral lobe and isthmus. But the removal of the isthmus is, after all, a small matter.

Approaching now the question from the point of view of danger, the real reason why any operation is dangerous, it seems to me, is because the diagnosis is imperfect. It is exactly the same as with cerebral tumour. Operation *per se* is not dangerous; it is that the operation is not used fairly as treatment but as a *dernier resort*. I agree with Dr. Dunhill in his series of thirty-two cases of exophthalmic goitre published in the Australian Medical Congress* last year, where he says that these cases must be brought to the surgeon before they have begun to go downhill. All cases of danger have been undoubtedly cases which were very ill for operation in the first instance. Consequently if you look at it purely from the surgical point of view, there is no danger provided the operation is conducted according to modern rules. I ought to touch, in relation to this question of danger, on the subject of anæsthesia. Here fashion is very apt to play a part, and without any disrespect to our Swiss colleagues, because in Switzerland they do not make a practice of having an expert class of men as anæsthetists, quite as much from that point of view I think as well as any other, Professor Kocher now operates without any general anæsthetic. My own experience has been that there is no trouble whatever with general anæsthesia provided you employ chloroform by the dosage method, which I think should be employed in all operations instead of the old mask, and provided, again, that oxygen is administered. The net result is certainly far more comfortable to the patient. Any of you who have seen private patients who have been operated upon abroad will realise that the local anæsthesia method is not comfortable to the patient. Neither do I think it is desirable in a patient who is extremely nervous. And as regards the extra point of knowing by the voice of the patient that you are not injuring the recurrent laryngeal nerve, I would only say I am not aware of having injured the recurrent laryngeal nerve in any case, and the little asthenic voice or hoarseness which sometimes follows the operation is certainly not due to direct injury of the nerve. So I cannot see any advantage in the employment of local anæsthesia, but many of my friends do employ it, and I have only thought fit to raise the point in connection with the question of danger, because though general anæsthesia is put forth as an extra source of danger, it is, I believe, an imaginary one. There only remains, then, one class of case upon which more ought to be said from a surgical point of view, and that is the desperate case. What shall we do for the desperate case? Because the desperate case will infallibly die. I speak of the case which is emaciated to the last degree already, has a temperature of 100°, 102°, or 103° F., and in which the nerve symptoms are extreme. It is clear we cannot operate in the way I have just suggested. I think that in future we ought first to transplant a portion of the normal gland. Normal gland grafting is of course a matter of convenience, and when I remove an adenoma if I have the patient on whom I wish to graft the thyroid, having excised the margin of tissue round the abdomen, and which is really normal tissue as it is not part of the adenoma, I employ it as a graft by Eiselsberg's original method, *i. e.* into the retroperitoneal tissue behind the upper part of the rectus I think that an extreme exophthalmic goitre patient, a desperate case, is suffering from athyroidism as well as from aberrant thyroidism. Therefore we should treat the athyroidism by grafting, because it is well known that thyroid medication by the mouth is of no use and makes the patient worse. We should graft in normal gland, and after a couple of months or six weeks have passed and the condition improved we could then deal with the exophthalmic goitre in the ordinary way. This is not merely a theoretical consideration; I have two cases which have been successfully compensated by grafting.

Finally, I wish to say a word on the iodine question, because I was surprised the other night to hear that point raised from the medical point of view. I am not one of those who believe in the exact parallelism between efficiency of the thyroid glands and the presence of iodine. Of the presence of iodine there can be no doubt, and the recent very elaborate and most interesting paper by Dr. Marine and Dr. Williams, of Cleveland, Ohio, on the question of thyroidal hyperplasia, and the fact that the non-colloidal contents become more liquid,

* See also 'Brit. Med. Journ.,' May 22nd, 1909.

and the iodine diminishes, naturally attracts attention to this point; but medication by iodine fails in exophthalmic goitre, and iodine consequently cannot play the *rôle* it has been assumed to do. I want to say one word more about iodine: I say it fails internally. But now comes the question of its external use, because one constantly sees cases in which when the goitres appeared they were painted with iodine. The surgeon knows if a case has been energetically treated with iodine, because he finds more adhesions between the goitre and the subhyoid muscles, and it occurred to me, in a simple adenoma which was thus adherent in front, to prepare one or two micro-photographs to show what happens in the gland when the exterior of the neck has been treated with iodine. In the first place you see that this is an adenoma of the normal type, but in which the colloidal secretion is getting older, and that the whole capsule in front becomes adherent by these large masses of tissue. Such an effect must be the consequence of intense congestion such as the skin constantly suffers under iodine. I would draw your attention to a small point with regard to the alteration of the colloidal secretion, namely, that in some of these superficial acini which have come under the compressing influence of the cicatricial contraction the colloidal material is almost crystalline. The adhesion is grossly magnified in this slide, but it shows the tough fibrous tissue of which it is formed. Further, in a single acinus there is the story of what has been going on in the gland. In the colloidal material of the acinus are caught up the cells which demonstrate the irritation which the gland has suffered. The colloid secretion is full of large and small phagocytes containing blood-pigment, showing that the only effect of the iodine was to produce a congestive condition of the surface, ending in plastic centralisation. I hope, therefore, that the day of treatment of all kinds of goitre by painting with iodine is past, and that it will be abolished like bleeding and sundry other barbarous methods of treatment.

I thank you once more for your courtesy in enabling me to take part in this discussion.

Mr. James Berry: Sir, I have to thank you and the Society for the honour you have done me in asking me to speak on this important occasion.

I feel that the subject of the operative treatment of exophthalmic goitre is one of much interest and importance and of no little difficulty.

There is still some uncertainty as to the exact pathology of the disease. There is by no means unanimity among authorities as to its clinical symptoms. There is still more divergence of opinion as to the desirability of surgical treatment in well-marked cases of this affection.

Our difficulties are enhanced by the unsatisfactory nature of the terminology employed by various workers. As Sir Victor Horsley said just now, we do not know exactly what is meant by the expression "exophthalmic goitre."

We find that some surgeons include under this term only the ordinary typical cases with the classical exophthalmos, rapid pulse, goitre, tremor, and other well-known symptoms. Other surgeons embrace under the same heading a large number of cases in which one or more of these symptoms, and especially exophthalmos, is wanting. Most of these are cases which I personally, and I think most of us, would not put into this category at all. The inclusion or exclusion of such cases, "*formes frustes*" as they have been called, make a very great difference to the statistics of the results of operation for exophthalmic goitre.

I will quote, for instance, the definition which Professor Kocher gives of the disease. In the address delivered by him at the Medical Society* three years ago, he said: "What I mean to sum up under the name Graves' disease or Basedow's disease includes all the affections in which the symptoms including the most constant goitre and heart trouble are dependent directly on the alteration of thyroid tissue and thyroid function." Such a definition allows us to include under these terms a great many cases in which there is no exophthalmos at all. Kocher expressly says: "Exophthalmos is frequently absent at the beginning of the disease, and may be absent for a long period."

According to this definition of Kocher's it seems to me to be very difficult to know what clinical symptoms are to be considered as pathognomonic of the disease. Personally, when I speak of exophthalmic goitre I always mean a disease in which there is both goitre and exophthalmos, and it seems to me that this is the only logical way of using the term. When these two physical signs are present most or all of the other symptoms are

* 'Med. Soc. Trans.,' 1906, vol. xxix, p. 373.

present as well. Palpitation and tremor without exophthalmos have been present in numbers of my operation cases. Such cases are often completely curable by operation, but personally I do not apply to them the term "exophthalmic goitre."

As to pathology, I accept the view that the disease is primarily one of the thyroid gland. In the thyroid gland alone do we always find definite pathological changes associated with the well-marked clinical symptoms which constitute a typical and unmistakable case of Graves' disease. These changes may be summed up as increase in the epithelial elements of the gland with diminution of the amount of colloid present in it. It has consequently been assumed that the essential cause of the disease is an over-activity of the gland, causing increased secretion of colloid. But it is assumed that the colloid, instead of accumulating in the gland as under normal conditions, is too rapidly absorbed. Some authorities consider that the term "hyperthyroidism" should be substituted for that of "exophthalmic goitre." This simple view of a mere over-activity of the gland will not, however, explain all the phenomena of the disease. If the gland were simply over-active, then a mere removal of a portion of it ought to be followed more often and more certainly by the cure of the disease than is actually the case. My own view is that the cause of the disease is not merely an excessive, but rather a perverted, secretion of the thyroid. I have known patients who have undergone more than one extensive operation for removal of large portions of the gland, patients in whom after operation scarcely any thyroid tissue remained, and who, nevertheless, continued to suffer from clinical symptoms of the disease. Indeed, in some cases the operations have been so thorough that actual myxœdema has ensued. I have never seen a post-mortem upon a case of Graves' disease in which well-marked persistence or hypertrophy of the thymus was not present, and I have seen several such post-mortems. Thorbecke* stated that out of thirty-six autopsies in cases of Basedow's disease, persistence or hypertrophy of the thymus was found in no less than 79 per cent. The meaning of this thymus change, whether it has a causal connection with the disease or whether it is of a compensatory nature, is, I believe, still wholly unknown.

Dr. Charles Mayo, of Rochester, U.S.A., whose work is doubtless well known to all of us, and for the excellence of whose work in this branch of surgery I have the warmest admiration and respect, has operated in the last few years upon a large number of cases of what he terms "hyperthyroidism," and in some of his publications he uses the term "exophthalmic goitre," and in others the term "hyperthyroidism." Like Kocher he includes in his statistics many cases in which exophthalmos is not present. In the recent admirable pathological report of his cases by Dr. Louis Wilson,* which I have in my hand, there is an exceedingly good description of the various conditions of thyroid found at his operations. From this we see that some of the cases present the ordinary type of Graves' disease. Others, however, appear to be examples of a condition of thyroid with which everyone who operates much upon the thyroid must be quite familiar. It is often found in ordinary chronic goitres. By ordinary goitre I mean an innocent goitre which is not associated with exophthalmos. I speak with a tolerably large experience of such operations, as the total number of my operations for removal of goitres of all kinds amounts at the present time to 495. Among these there are many in which the microscopical appearances were precisely similar to those depicted in some of Dr. Wilson's later illustrations. Nevertheless I should hesitate to call these examples of true exophthalmic goitre. In the last report of Dr. Mayo's Hospital we read that in 1908 as many as 239 cases of "exophthalmic goitre" were operated upon, partly by thyroidectomy and partly by ligation of arteries. Of these 239, not less than 180 are stated to have been cured, 51 were improved, 4 were not improved, and 4 died. If we could consider all these cases to be really genuine cases of exophthalmic goitre, this would truly be a most remarkable record. I am afraid we must conclude, however, that many, perhaps most, of the cases were not exophthalmic goitre in the ordinary sense.

When we turn to Professor Kocher's statistics

* "Der Morbus Basedow mit Thymuspersistenz," 1905; quoted by Capelle in 'Beitr. z. klin. Chir.,' 1908, vol. lviii, p. 353.

* "The Pathological Changes in the Thyroid Gland as Related to the Varying Symptoms in Graves' Disease, based on the Pathological Findings in 294 Cases," 'Amer. Journ. of Med. Sci.,' December, 1908.

we find that he also appears to include under this term many cases in which the diagnosis would not agree with that which I think Sir Victor Horsley would have made. Professor Kocher divides his cases into three different classes, but speaking even of the class which he calls that of "typical exophthalmic goitre," he lays stress on the fact that many cases have no exophthalmos! His results in the 106 operation cases of this class were that nine died, nine were greatly improved, seventeen were either better than before the operation or were cases recently operated upon from which he could draw no conclusion, and sixty-two were cured. Here is another element of confusion, for what is meant by "cured"? I notice that sixty-two are put down in Kocher's statistics as "cured," and it is stated that thirty-four of these were "perfect cures." One may well ask what is the difference between a "cure" and a "perfect cure."

Besides these gross statistics, as I may call them, of which we hear so much, there is another more valuable source of information open to us in the detailed reports of cases of operation for exophthalmic goitre. Reports of isolated cases are of comparatively little value in enabling us to come to a definite conclusion as to the desirability or not of operation for this disease, or as to the mortality of the operation. In our own language I do not know of any very large series of consecutive cases in which each case is described in full. But there are several such series in German medical literature, and they are of the utmost value to us.

Dr. Witmer, for example, has published in full a long series of consecutive cases operated upon by Prof. Krönlein at Zurich.* There is also an admirable monograph† by my friend Dr. Albert Kocher, of Berne (Prof. Kocher's son), who has given at most extraordinary length, and with most minute details, the particulars of a long series of cases operated on by his father. I confess that the impression left upon my mind after reading through many such papers is that although you can get very good gross statistics about exophthalmic goitre if you employ this term sufficiently loosely, yet when it comes to dealing with bad cases of genuine exophthalmic goitre (and these are the very cases upon which we should like to operate were it reasonable to do so) the operations do not seem to be very satisfactory. The patients are often improved, sometimes remarkably so; occasionally they appear to have been really cured by the operation. But if you follow up the cases you will often find that the improvement did not last, or else that it was only after a long period of years that the patient was cured. Often second operations are performed for the removal of more thyroid gland, but even then cure does not necessarily follow. The reading of such literature makes me feel extremely doubtful whether, on the whole, operations for the removal of typical exophthalmic goitre really do much good. Let me give you a few details. In the 'Medical Annual' for the current year* reference is made to the results obtained by Professor Garré, the well-known surgeon of Bonn. His operations for Basedow's disease, twenty-eight in number, have been described in full detail in an excellent paper by Dr. H. Moses.† Now, the 'Medical Annual' simply says that of these twenty-eight cases "four were cured, ten were so much benefited that they could return to work, six were only slightly benefited, three were not improved at all, one died." Looked at in this way these statistics seem fairly satisfactory. But if we read the original paper which I have here, we are struck by the fact that a considerable number of the cases are what Moses himself calls "secondary cases," cases in which there is no exophthalmos at all.

Discussing this very question whether the cures occur only among the secondary cases, he can bring forward only two cases of "undoubtedly genuine" Basedow's disease in which the operation was followed by cure. From the description given of the pathological findings in these cases there seems no doubt that these two were really genuine cases. But two cases out of twenty-eight is not a large number.

A third source of information from which I venture to draw conclusions is that of my personal experience of patients whom I have seen before operation and patients I have seen after they have

* 'Beitr. z. klin. Chir.,' vol. xxix, pp. 191–243.

† 'Mitteil. a. d. Grenzebiet. d. Med. u. Chir.,' vol. ix, 1903.

* P. 345.

† "Beitr. z. chir. Behandlung d. Morbus Basedowii," in 'Beitr. z. klin. Chir.,' 1907, vol. lvi, pp. 524–580. "Basedow's disease" is, of course, the ordinary German term for what we call "Graves' disease."

been operated upon by others, sometimes both before and after operations which I have seen done by others. The conclusion I have come to with regard to these is also that the evidence in favour of operating in ordinary Graves' disease is not very strong.

I alluded just now to the cases of atypical exophthalmic goitre, which so many operators include in their statistics of operations for exophthalmic goitre, and of these I have operated upon a considerable number. I am quite willing to admit that in my narrow limitation of the term "exophthalmic goitre" I may be quite wrong, and that I ought to include many of these other cases under the same term. I will take two cases at random from my operations as illustrations of what I should call false exophthalmic goitre. Miss X—, æt. 25 years, was sent to me by a doctor, who wrote: "She has been under my care suffering from Graves' disease for the last three years. It began in July, 1904, after the death of her father," and he then goes on to mention the symptoms: "thyroid enlargement, slight exophthalmos. rapid pulse, tremor, breathlessness after exertion, etc. These symptoms have continued ever since"—that is to say, for the three years which elapsed between the beginning of the disease and the time when I first saw her. "She has had every kind of treatment, medicinal, climatic, general and local, everything that I know of." She was seen twice by a well-known London physician, and was advised to go to Berne, to Dr. Kocher, with a view to operation." This she did not do. Absolute rest in bed for four months was then undertaken. "Some diminution of the symptoms certainly resulted, but afterwards she was worse than before." She then saw a well-known physician in Birmingham and was sent by him to the seaside for some months. I myself first saw her in December, 1907, and I found she had an encapsulated cystic adenoma of the right lobe, a perfectly ordinary cystic adenoma, such as one has seen by the hundred. She had also a pulse-rate of 132—a by no means uncommon thing in simple goitre. The exophthalmos alluded to in the letter was not more marked than I have seen in many normal people. Her sister told me the eyes had always been as they were when I saw her. I said that I did not consider the case to be one of true Graves' disease at all, and I expressed the opinion that removal of the tumour would completely cure her. I did a resection-enucleation a few days later, and she made an ordinary rapid uneventful recovery. She left the Home ten days after the operation with a pulse-rate of 80 to 84. Six months afterwards her doctor wrote to say that her recovery was "perfect." Since then I have seen her myself and found her quite well. Her doctor was an experienced and able practitioner of thirty years' standing, and the consultants who saw her were well-known physicians. You may say that this was a case of genuine exophthalmic goitre, and that I did not recognise its true nature. However that may be, the practical point is that this is the kind of "exophthalmic goitre" that is easily curable by operation.

Another case I should like to mention is that of a lady, æt. 33 years, whose doctor wrote to me that he was bringing a patient "suffering from Basedow's disease." In this patient, as in the last, I found an encapsulated adenoma of one lobe, and I do not know why the case was thought to be Basedow's (*i. e.* Graves') disease, except that at times she had some palpitation and rapidity of pulse. She had been seen by a distinguished London physician, who considered she had Graves' disease. Her brother, who was a doctor, had also, I was told, arrived at the same conclusion. I told her that her tumour could easily be removed and with little or no danger, but in the face of three opinions to the contrary it is not surprising that she did not submit to any operation. Seven years later, namely in 1907, I saw her again; she was then in the same condition as before, but the tumour was larger. She said that if I could assure her she had not Graves' disease she would have the operation done; she was anxious for it. I readily gave her this assurance and removed a cystic adenoma as big as a large orange, and she was well in a few days. She has remained well ever since. That was a case in which the fear of the operation for Graves' disease had led to this unfortunate lady carrying her goitre about unnecessarily for seven long years.

Now assuming, as I am afraid I must, that a very large proportion of the so-called cures of exophthalmic goitre occur in people who have not got genuine Graves' disease at all, there remain undoubtedly many genuine cases of the disease that are operated upon by some surgeons. To the

question what are the results of operation in these cases I find it extremely difficult to give a definite answer. Most operators seem to agree that typical bad acute cases are best left alone. I may say that a good deal can be done for such cases in my experience by medical means alone, and especially by the administration of sodium salts. It is in these acute cases that operations are so particularly dangerous, and yet it is just these bad cases that I am so often asked to operate upon. The more chronic cases are, however, more suitable for operative treatment, provided that the heart has not been too much enfeebled by prolongled overwork. I have in my mind a man, æt. 32 years, who was sent to me some years ago by Dr. Harry Campbell, with most pronounced symptoms of Graves' disease, which had existed for a considerable time. He had exceedingly marked exophthalmos, palpitation, rapidity of pulse, tremor, emaciation, diarrhœa and extensive bronzing of skin. He was so nervous and excitable that he had for some months been wholly unable to follow his occupation, that of a clerk. He told me that he was anxious to undergo any operation, however dangerous, which would afford him any prospect of relief. In July, 1901, I tied both superior and one inferior thyroid artery under local anæsthesia, and within a few weeks a most extraordinary improvement set in. His palpitation almost entirely disappeared, his pulse-rate fell markedly, the diarrhœa disappeared, and he lost practically all his subjective symptoms. He was able after a few weeks to return to work, and although he never completely lost the exophthalmos, and was liable to occasional attacks of palpitation during excitement, he was practically well, and always expressed himself as most grateful for the great amount of benefit he had derived from the operation. When I last saw him, fourteen months after the operation, he told me that he felt quite well and "was able to do his work as well as anyone else." His weight, which before the operation was only 5 st. 4 lb., increased to 9 st. 7 lb. He remained at work till the day of his death, some time afterwards. He died suddenly in an epileptic fit. He had been subject to epilepsy for many years before his exophthalmic goitre began.

Such improvement may be expected in many cases, and although not amounting to cure nevertheless does largely justify operations. But complete cure in such cases is certainly rare.

Not long ago I happened to meet the first assistant of one of the best known Continental operators for Graves' disease. Having got to know him fairly well I said to him: "Now, tell me, what is your experience of Dr. So-and-So's operations for exophthalmic goitre; are his cases really cured?" He smiled, shurgged his shoulders, and said: "Well, they are improved," and that was all he could say.

The chief danger of operation on the thyroid where palpitation and rapid pulse are prominent features is great restlessness followed by heart failure. Excessive rapidity of the heart's action after operation in such cases is best treated by massive saline infusion, administered slowly *per rectum*.

I have said nothing at all about two other operations which have had much said in their favour, although I think undeservedly. One is division of the sympathetic cervical nerve, and the other is exothyropexy. Neither of these is worth doing. I have seen resection of the sympathetic performed at a London hospital for a very ordinary case of Graves' disease, and the patient died in a few hours with the usual symptoms of restlessness and rapid pulse. Exothyropexy, as far as I know, has never been done in this country. It is a barbarous and dangerous operation, and one which I do not suppose any of us would be inclined to perform.

The conclusions at which I have arrived in regard to the surgical treatment of Graves' disease are the following:

Bad acute cases of typical Graves' disease should seldom be operated upon. If operation is undertaken it should only be done after a prolonged course of medical treatment. Operation of any kind in these cases is usually exceedingly dangerous to life, and the prospect of complete cure is by no means very hopeful.

The more chronic cases of Graves' disease involve much less risk of an immediately fatal result. Such cases often benefit in a remarkable manner from operation, either ligature of thyroid vessels, or excision of a part of the gland. Cure is, however, by no means certain or complete.

Cases in which there is dyspnœa with stridor almost invariably demand operation. There exists a large group of cases of goitre in which some of the symptoms of Graves' disease are present, notably tachycardia, palpitation, tremor, sweating and emaciation, but without marked exophthalmos. Such cases are eminently suitable for operative interference, usually by unilateral extirpation or some variety of enucleation.

In many of these cases the goitre is more or less unilateral. The operation, if performed with due precautions, involves comparatively little risk to life, and is almost invariably followed by complete cure. Some of these cases are those of simple goitre of long duration in which the Graves-like symptoms have only recently been present. I have operated on many cases of this class, and never yet lost one of them. Personally I do not apply the terms "exophthalmic goitre" or "Graves' disease" to cases of this class, although many others do.

(*To be concluded.*)

August 2nd, 1909.

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A CLINICAL LECTURE

ON

ASTHMA.

Delivered at St. Bartholomew's Hospital.

By SAMUEL WEST, M.D., F.R.C.P.,
Physician to the Hospital.

Gentlemen,—I am going to speak to-day about asthma and its treatment. To understand the treatment of any disease it is necessary to agree exactly upon what is meant by the term. The more we know about a disease the more indications we ought to have for the treatment of it, and the more likely we shall be to be able to deal with it in a rational way. And that is especially true with regard to asthma. In the first place, then, what do we mean by the name? It is quite certain that the term is very often misapplied. You often hear people talk about asthmatic conditions, cardiac asthma, bronchitic asthma and so on. For instance, if a patient has a weak heart dyspnœa may occur, and come on in paroxysms. These attacks are sometimes called "cardiac asthma." They should be described as "cardiac dyspnœa," for they are not asthma.

In the same way in the course of bronchitis dyspnœa may set in suddenly, or become suddenly aggravated. This dyspnœa has been called "bronchitic asthma," but it is due to the mechanical obstruction of the air-tubes by the secretion, and is, again, not asthma at all.

Paroxysmal dyspnœa, again, may be associated with enlarged glands in the mediastinum—a condition not uncommon in children and not altogether rare in the adult. If the bronchial glands get inflamed they will swell rapidly, just as they are often seen to do in the neck. The enlarged glands may then cause pressure on the large air-tubes and cause dyspnœa.

Plastic bronchitis is another affection which is often confused with asthma. In this disease casts form in the bronchial tubes, and as the casts are forming there will be gradually increasing dyspnœa, which will be immediately relieved when the casts are expectorated. The casts may form day after day, and the attack of dyspnœa be thus curiously periodic. If the casts take longer to form the interval may be irregular and the attack be continued for a considerable time. A marked case of this disease is not difficult to recognise, but in milder cases the diagnosis is not easy, and I have seen many cases of plastic bronchitis which have been diagnosed and treated as asthma. Plastic bronchitis can frequently be rapidly cured by large doses of iodide of potassium, but if the condition has not been recognised this treatment will not suggest itself.

True asthma is a very peculiar condition. If you examine a patient in an attack you will find that the chest is more or less rigid, in the position of deepest inspiration, and moves but little. If you take the fullest breath you can draw and fix your chest in that position you have it in much the same position as that of an asthmatic patient. The chest is expanded and the diaphragm pushed down, and if you now take just short breaths, releasing the chest from that position as little as possible, you will understand what discomforts are suffered by a person with asthma. Asthma is a respiratory defect; there is very little expiratory oscillation of the chest. Instead of a proper oscillatory movement of the chest there is simply a flickering expiration, so that there is very little interchange of air in the lungs, the air is imperfectly oxygenated, and the patient becomes blue in the face or deeply cyanosed. The abdominal muscles are also affected to some extent. It is not simply a chest affection, nor simply a diaphragm affection; there is no particular obstruction in the larynx; it is an affection of all the inspiratory and some of the expiratory muscles, and there is in addition a spasm of the bronchial muscle.

Where can the lesion be which is capable of exciting such widespread effects? Clearly not in the lungs, so that asthma is not a lung disease although it is a respiratory affection. Such an extraordinary widespread spasm or rigidity of these muscles must be controlled from some part of the central nervous system. Asthma must therefore be a nervous disease, and as there is no organic lesion to be found it is called a "respiratory neurosis," "neurosis" being a term of general application which implies that it is a nervous affection without known organic lesion.

There is another respiratory neurosis which is called "hysterical asthma," but that is a complete misconception of terms. Whatever we may exactly mean by hysteria we may be certain that hysterical asthma is neither hysteria nor asthma. No one will confuse the two conditions if he remembers that in asthma the chest is fixed, whereas in hysterical asthma so-called, although the rate of breathing is great—80 to 100 a minute sometimes—the respiratory movement is excessive, and instead of dyspnœa and cyanosis the patient has hyperpnœa, with a red face and a highly oxygenated condition of the blood.

You see the theory now that we must adopt. We must regard asthma as an affection of the nervous system and not of the respiratory system at all. And Hughlings Jackson, many years ago, called it a "respiratory convulsion," and compared it with epilepsy. That is a very instructive comparison. The diagram which I give you may be applied equally well to either asthma or epilepsy.

Asthma is a general nervous condition, which for our present purposes we may represent by a circle or centre—there is, of course, really no such centre. We do not talk about an epileptic centre, but we do talk about an epileptic condition, and as there is a condition of the nervous system which is essential if epilepsy is to occur, so there is apparently a similar condition for asthma. This condition or centre may be excited in various ways. It can be excited from the brain, and there are cases which are closely related to insanity. In other cases it may be brought on by emotion, *e.g.* a shock or fright and excessive immoderate laughter. Sometimes the asthmatic paroxysm is excited through the special senses, *e.g.* smell, sight, or hearing. I remember a lady who always had an attack of asthma if she sat with her back to a draught, and it was frequently produced experimentally by blowing sharply on the back of her neck. Asthma stands in some relation to skin eruptions, and some authors hold that asthma depends on a certain urticarial or sudden swelling of the mucous membranes of the air-passages. Paroxysmal dyspnœa resembling asthma to some extent may

sometimes be produced in this way, but it is not true asthma.

There are some conditions which perhaps affect the centre itself, and are the result of the circulation through it of blood containing toxic substances, uræmia for instance, and this is what is meant by renal asthma. In a similar way the centre may be excited by the crude products of imperfect digestion; this represents what has been called peptic asthma. Nothing is commoner than this, so that asthmatic patients have to be extremely careful about the diet, and they can often tell you what particular foods disagree with them in this respect.

In other cases the irritation may be connected with the vagus nerve. The vagus is connected with the heart, with the lungs, and with the stomach, and so there has been described a cardiac asthma, a bronchitic asthma, a dyspeptic asthma, and so on. Now if in the diagram I substitute for asthma epilepsy, you could use the same scheme.

In most of the cases epilepsy is associated with an aura as a preceding phenomenon. There may be sensory auræ—sight, smell, or touch; emotional auræ—as fright, excitement, anger, etc. Epilepsy may be quite an early symptom of kidney disease, and gastric and intestinal dyspepsia often precede an attack.

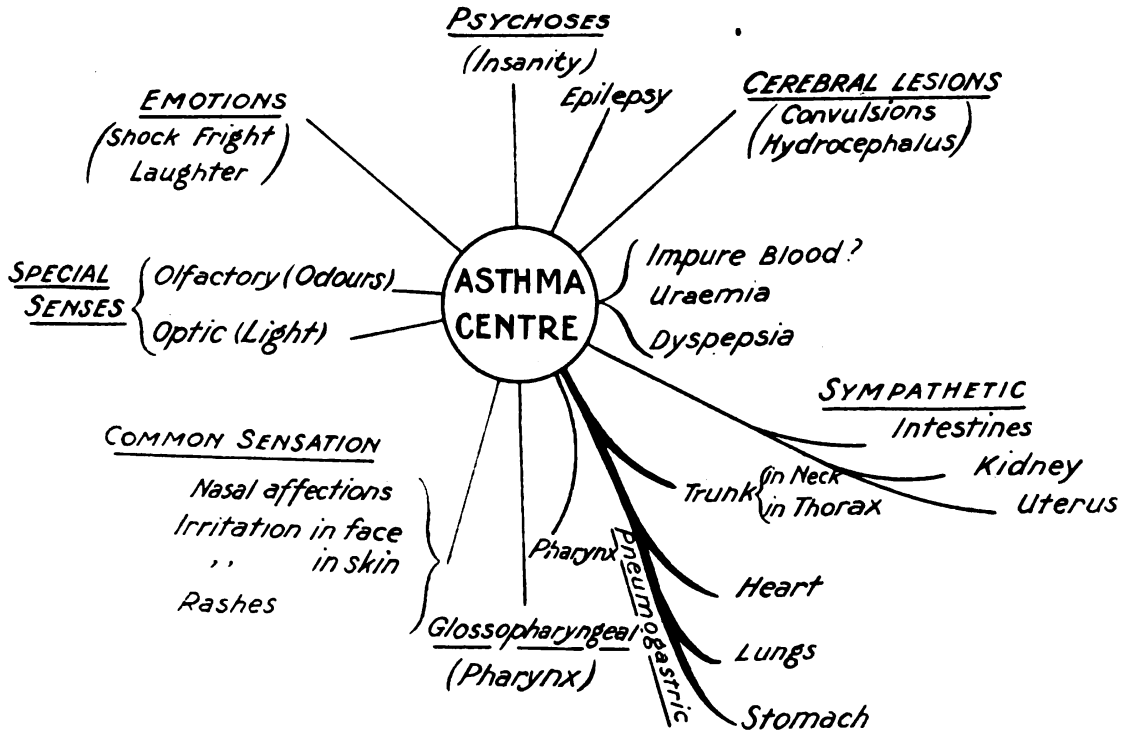
This scheme, therefore, will impress on your mind the fact that asthma may be fairly described as a neurosis.

As in epilepsy, so in asthma the aura or antecedent premonitory symptom is of importance in regard to the treatment, so that the diagram may constitute as well a sort of peg on which to hang indications for treatment.

In epilepsy, supposing the patient seems to have a twitching in the thumb or a curious sensation in the foot—and many of them do in epilepsy—then they can often, by tying a bandage round the thumb or pulling a garter round the leg tight, cut short an attack of epilepsy. So in some of these cases of asthma, when the patients recognise, as they often do, symptoms of an oncoming attack, appropriate methods of treatment if carried out will often stop an attack. So it is important to study each case and find out what premonitory indication there is, because, of course, it is better to prevent an attack than to let it develop and then treat it.

The treatment of asthma, then, falls naturally into two categories. We have to treat the asthmatic

FIG. 1.



paroxysms, just as we treat an epileptic fit, and we have also to treat the general condition upon which the asthma depends, just as we endeavour to treat the general condition upon which epilepsy depends.

We will take first the paroxysms. You cannot do very much for a patient who has already an epileptic attack at the time, except preventing him from injuring himself and doing all you can to relieve the intensity of the symptoms for the moment. As soon as the immediate attack is over, you can begin to think and decide how to treat him in such a way that he will not have another attack. It is the same with asthma.

What shall you do with the paroxysm of asthma? There are three lines upon which you can go. You can give drugs of some kind which will soothe the excited centres or general condition. Then you can diminish or treat in various ways any peripheral source of irritation which may have brought the attack about, or which may be associated with the attack. And thirdly you can give the patient various remedies which will relax the spasm. To reduce the excitability of the centre some sedative may be given, *e. g.* chloroform to inhale, or some rapidly acting narcotic, of which of course opium or morphia are the most certain. But as asthma is a disease which lasts a long time, and the patient is constantly liable to develop these attacks, there is a great danger of the patient acquiring the chloroform-habit or the opium-habit. So it is best not to use these remedies if they can be avoided, but to try other things first. Still we may be driven to them after all, because the patient's suffering is often intense, and cannot be relieved in any other way.

There are many other drugs which check the paroxysm. I have already suggested that the circulation might have something to do with the development of the attack, and some of the drugs which are found beneficial act on the heart and blood-vessels. Among the most useful of these drugs is caffein given by the mouth or by subcutaneous injection. A cup of strong black coffee is a traditional remedy for asthma, and its effect probably depends on the caffein which it contains. Another useful drug is nitrite of amyl; this rapidly produces great vascular dilatation and may give immediate relief. Iodide of ethyl often does good. It is a volatile substance, and contains a large amount of iodine which is readily absorbed in this form. Pilocarpin is another drug which sometimes acts when others fail. This acts on the vessels and relieves spasm. Another drug which has an exactly opposite action, and yet is useful, is adrenalin.

Now let us take the other indication: How shall we relax the respiratory spasm? Of course chloroform is the best thing, and opium is another good thing, but there are the same objections to them which I have urged already. Another class of remedies which will relieve the spasm are depressants. Ipecacuanha and lobelia are two such drugs, especially the latter, which are found useful. But they are distinct depressants, and so is nicotine.

Next we may attack the peripheral irritation, upon which probably the asthmatic attack depended. Some asthmatic attacks are brought on by irritation in the bronchial tubes; at any rate they are often associated with a good deal of irritability of the bronchial nerves at the time of the attack, and inhalation is the most useful way of applying many of the remedies to which I have referred. Local sedatives, such as cocaine, belladonna, and chloroform may be applied in the form of a spray.

The most popular way of using many of these remedies is inhalation, and I have brought down a few things for you to try upon yourselves. Here is some nitrite of amyl. A little time after you inhale this, after a preliminary cough you will perhaps blush, showing that a relaxation of the vessels has taken place. Here is some iodide of ethyl, which contains a good deal of iodine, and is a ready way of introducing iodine into the system. The common fumes for inhalation are derived from nitre papers, *i. e.* blotting-paper soaked in nitre so as to make "touch-paper" of it. With this all sorts of drugs may be combined, such as arsenic and belladonna. The proper way to administer these inhalations is not in a large room like this, but in a more or less closed box, or with a towel round the head or under an umbrella. Many of the asthma cigarettes sold are made from these nitre papers rolled up and impregnated with various drugs. There is one group of remedies which has a very important action, the atropine group, such as stramonium, belladonna, atropine. Many of the asthma powders consist of these drugs pounded up and mixed with nitre. These are then put into a pipe or saucer and set fire to; they will smoulder

for a long time. Here is a powder consisting of a mixture of belladonna, digitalis, and stramonium leaves. All sorts of names are given to these powders—Himrod's powder, Bliss's cure, etc.—but essentially they differ very little from each other.

"Bronchitic asthma" is a common term, as I have said, and there is a form of true asthma which comes on from irritation of the bronchial tubes. But the dyspnœa which comes on in the course of bronchitis is not asthma, and if you give these smokes for a patient to breathe when he has bronchitis you will certainly not make him any better. I remember a bad case which was said to be one of asthma, and in that case smokes and powders of every kind had been tried. The fact was that the patient ought not to have had any of them; they were stopped; the bronchitis at once got better, for it was that he was suffering from and not from asthma.

There is another remedy which has been before the public a good deal lately, and that is "Tucker's Cure." "Tucker's Cure" does good, but it is not anything specially to do with Tucker. Nearly all the chemists make preparations of a practically similar character. They consist of a spray of liquid paraffin or parolein with a variety of substances dissolved in it. Nearly all these preparations contain cocaine. The materials are given in a very simple way: the tube is put into the nose and a breath taken and the ball is squeezed sharply, thus projecting the spray into the nostril. The objection to all these drugs, and especially to cocaine, is the danger of the drug-habit forming. When used so often it is astonishing how much cocaine may be inhaled during the day. Such a practice cannot be wise. Sprays, in order to do good, must be given in the proper way. To open the mouth and direct the spray in is no good, for then the spray is simply deposited on the pharynx. The best way to spray is through the nose, the patient taking a deep breath just at the right time and then a good deal will get into the air-passages, at any rate into the main passages.

The third thing in asthma to treat is the general condition. How can such patients be kept free from attacks? If there be an irritable condition of the nervous centres similar drugs to those used for epilepsy may be given. Bromide of potassium is being largely used for the condition, but iodide of potassium is more useful in asthma than is the bromide. But a combination of bromide and iodide of potassium is excellent, and if patients who are subject to these attacks are given this mixture they may have no attacks for weeks or months, though previously they may have been having them at frequent intervals.

Next there is the prophylactic indication: if the patient cannot stand the presence of a cat in the same room, cats must be kept away. If the patient cannot stand certain sights and smells or excitement of various kinds you must do your best to save your patient from these excitants; but such measures patients often prescribe for themselves.

Another important point which has to be borne in mind is locality for a residence. Asthma is the most extraordinary disease there is in that way. A patient who is subject to asthma may be able to live comfortably on one side of a street but not on the other, on the third storey of a building but not on the ground floor. I once had a patient who could not live at Whitechapel and had to change the residence to Wapping. Some asthmatics are never so happy as when they are breathing a thick London fog, which of course is not a joy to most people. Others used to enjoy travelling on the old sulphurous Metropolitan and District railways, because it gave them so much relief. No one can tell offhand where an asthmatic patient should live. Various localities must be tried till one is found to suit, so it is no good to suggest heroic travels and long journeys. One thing to be borne in mind is that asthmatics are nearly always better in London than almost anywhere else.

The habits of the patient must be regulated. They must not live under conditions of emotional excitement any more than should epileptics. The diet should be carefully regulated, for an attack may easily be determined by some error or indiscretion in food, for asthma is a disease which in respect of causation bears some analogy to urticaria, and thus I knew a patient who could eat a cooked apple, but not a raw one. In these respects idiosyncrasy has to be reckoned with.

I do not attempt to give you minute details of treatment, but I have tried rather to indicate the lines upon which treatment should proceed, and to show that it is upon careful study of each individual case that success in treatment largely depends.

August 9th, 1909.

DYSMENORRHŒA.*

By THOMAS G. STEVENS, M.D., B.S.Lond., F.R.C.S.Eng., M.R.C.P.Lond.,
Physician, Hospital for Women, Soho Square; Physician to Out-patients, Queen Charlotte's Lying-in Hospital; Obstetric Tutor, St. Mary's Hospital.

THE problems connected with painful menstruation are at all times difficult to unravel, and often its treatment is so baffling as to make us despair of a cure in some particular case. We must not, however, forget in our efforts to overcome these troubles that a clear understanding of the physiology of menstruation will do much to assist us to elucidate difficult questions and do not a little to help us in the treatment of each case on its merits. Our knowledge of the physiology of menstruation has undergone some changes in recent years, and with the additions gained our therapeutic armamentarium is so much the more widened. The researches of Heape and others have done much to make clear what are the changes which occur in the endometrium during the menstrual flow and in the period which precedes the flow. In the intermenstrual period we recognise a time during which repair of the endometrium takes place followed by a preparation of the uterine mucosa for the next monthly loss. This preparation is essentially an increased blood supply leading particularly to the dilatation of the superficial capillaries around the mouths of the uterine glands, and accompanied by some slight thickening of the endometrium, the result of connective-tissue increase. These changes are really the preparation of the endometrium for the reception of a fertilised ovum, the congested, thickened mucosa forming a surface which is readily attacked and pierced by the trophoblast covering the early embryo. The failure to receive a fertilised ovum necessitates a relief of this congested mucosa, and this relief is obtained by the menstrual flow. The flow is essentially the result of a great rise of blood-pressure in the vessels of the uterus, a rise so great that the distended capillaries are unable to withstand the pressure and consequently give way. If a fertilised ovum is received and embeds itself this increased blood supply is used up in supplying pabulum to the growing embryo, and also to the great connective-tissue overgrowth which culminates in and continues as the decidua of pregnancy. The amount of endometrium which is cast off is practically *nil*, the menstrual blood finding its way out either between the epithelial cells of the lining, or by carrying away a few cells on the surface and so making a small opening. The menstrual fluid, therefore, consists chiefly of blood with very few cellular elements derived from the uterus, but accompanied by a large quantity of mucus poured out from the uterine glands. This menstrual fluid commonly does not clot and certainly never does in the uterus itself. If clots do appear they form in the vagina, and must be due to an increased amount of blood out of all proportion to the mucous flow. We assume that it is the admixture of mucus which prevents clotting, but our knowledge on this point is not precise at present.

The cause of these physiological changes in the uterus must be looked for in the bio-chemical stimulus provided by the internal secretion of the ovaries. This internal secretion is intimately related with those of the other ductless glands, namely the thyroid, supra-renal and pituitary, and no doubt the nice adjustment of balance between these secretions is largely responsible for the normal physiological working of the economy in general. The physiological congestion of the pelvic organs at the beginning of menstruation is usually accompanied by a vaso-constriction in the skin, and changes in other viscera such as the stomach and intestines may possibly occur. It is clear from this short survey of the menstrual process that comparatively small changes in the stimulus and in the organs concerned may suffice to disturb the balance of the normal, and produce abnormal conditions, of which pain may be one of the manifestations and an alteration in the amount of flow may be another. Thus within physiological limits a slight increase over the normal congestion of the uterine capillaries may lead to such tension in them as to produce pain followed by an increased flow, whilst a diminution of this congestive process may even result in no flow at all. This latter is apparent, for a certain degree of capillary distension and rise of blood-pressure is necessary before the vessels will give way; on the other hand, a very slight alteration in the walls of the capillaries themselves or in

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the texture of the connective-tissue stroma of the endometrium, may render it more difficult for the blood-vessels to give way under the normal physiological rise in blood-pressure. This must give rise to a temporary but appreciable increase of tension in the whole uterus and consequently pain results, for any organ the subject of unusual internal tension becomes painful. We have no histological data to guide us as to this hypothetical change in the capillaries or endometrial stroma, but there can be no difficulty in believing that in some individuals the capillary walls and stroma may be slightly more tough and resistant in texture than in others; the microscope will not assist us to recognise minor differences in texture such as this, but in my opinion it is well worth consideration. Again, it is not only the uterus we have to contemplate in solving this problem, for we cannot overlook the fact that the ovaries themselves may be at fault. The ovary shares in the general congestion induced in the sexual organs by the menstrual stimulus, and slight increases of blood-vessel tension in them may be a source of pain. Again, also, the Graafian follicle ruptures and ovulation occurs as a rule somewhere about the same time as the menstrual flow; we do not know if these processes are of necessity synchronous, but in general we know that they bear some relation to one another. Consequently, if there is some difficulty in the Graafian follicle rupturing, the amount of tension thus produced in the ovarian vessels may at least be a contributing factor in the causation of pain.

The general symptoms which we commonly designate by the term "menstrual molimen," including headache, gastric and intestinal disturbances, coldness of skin and extremities must not be overlooked as playing an important part in the pathology of painful menstruation. In the light of our present knowledge it is probable that these disturbances owe their origin in some way to the presence in the blood of the bio-chemical stimulus, the ovarian internal secretion, and possibly represent a disturbance of the relations between this secretion and the internal secretions of the other ductless glands.

The time consumed in the consideration of these physiological details is not wasted, for as we approach the clinical side of the question and touch upon the pathology of painful menstruation we shall the more readily understand how the physiological balance may be upset.

There is no new classification of the clinical cases as they present themselves and I know of no better headings under which to group them than the old ones, "spasmodic," "congestive," and "membranous."

The *spasmodic* type of case is by far the commonest which comes before us, and belongs especially to the unmarried or the married women who have no children. This is essentially a primary condition, that is to say, the pain complained of commences with the first menstrual period, but commonly gets worse as the patient becomes older. The character of the pain is well described by the word "spasmodic" in that it is not continuous, but comes and goes in a colicky manner very closely resembling the other colics in its essential characters. It is not true to say that the intervals between the spasms are altogether free from pain; there is always some continual aching, but this does not alter the general assumption that the character of the severe pain is spasmodic, griping or colicky. Further, the time at which the pain occurs is important. It is essentially menstrual—that is to say, it occurs during the flow or begins only a few hours before the flow is established. Accompanying this pain there may be tumultuous gastric and intestinal disturbances leading to vomiting or several quick actions of the bowels. The degree of pain complained of is very variable in different individuals, but is often sufficiently severe to make it impossible for the patient to rise from bed, and consequently to prevent her from following her business or going about her pleasures.

The explanation of this pain has been a source of difficulty from time immemorial, and much controversy has taken place concerning it. The character of the pain irresistibly suggests that it is due to painful muscular contractions, and all the evidence before us seems to point to this as an absolute fact. We differ, however, from the older writers in our interpretation of the cause of these painful contractions. It was assumed by the older authorities that these contractions were the result of the attempts of the uterus to expel its contents against some obstruction, and it was supposed that stenosis of the cervix was the obstructing agent, or perhaps in some cases an

acute bend in the cervix. Hence the term "obstructive dysmenorrhœa" arose. We now believe, however, that no such obstruction exists in the majority of cases, in fact, the only true obstructive dysmenorrhœa is due to cicatricial partial closure of the cervical canal after operation on the cervix, or following sloughing the result of injury. There is no difficulty in passing a sound into these uteri as a rule, and according to some authorities the sound passes more readily during menstruation than at other times. Further, as the contents of the uterus are fluid there is no theoretical difficulty in its passage through a cervix which will admit an ordinary probe. We must, however, remember that at all times the contents of the uterus have to be expelled by muscular contractions, even the menstrual flow or normal secretions. Fluid will not flow out of the normal cervix by itself, and the pathological effect of this is seen in those senile uteri the subjects of chronic endometritis accompanied by pus formation. In these cases, because the uterine muscle has atrophied the pus will not flow out, but collects and distends the uterus even to the amount of a pint of fluid, and this in spite of the fact that the cervix is patent. Thus a pyometra arises owing to atrophy of muscle and gradual distension of the fibrous uterine wall.

If, then, there is no obstruction to the outflow of fluid from the uterus, we must look to the uterine muscle itself as a cause of the pain. If we assume that the uterine muscle is weak or badly developed we shall have a theory which fits in well with the clinical aspect of the cases. For a badly developed muscle is unable to perform its allotted task in a painless manner, not only in the uterus but also in the voluntary muscles, and consequently we have no difficulty in believing that the uterine muscle acts in a painful and spasmodic manner during menstruation. The effect, too, of a badly developed uterine muscle is not confined to the mere expulsion of the uterine contents, but also has an important influence on the uterine blood-vessels. The blood-flow through the uterus is largely dependent for its normal characters upon a well-developed musculature, and if this fails the result will be over-distension of the veins and capillaries, more marked naturally during the menstrual congestion. It is possible that this over-distension of the vessels alone is sufficient to call forth irregular and spasmodic muscular action without any actual blood being present in the uterine cavity. This view, which was originated by Theilhaber, has much in it which appears convincing from the pathological side, and when we come to consider the natural history of these cases and the anatomy of these uteri we find considerable evidence in support of the theory.

Looking at the natural history of the cases we find that they occur in virgins or married women who have had no children. Further, we find that pregnancy and labour very frequently cures them. The reason for this must be looked for in the natural effect of pregnancy and labour on the uterus. Pregnancy leads to the greatest possible development of the uterine muscle and the greatest possible stretching of the lower uterine segment. It follows, therefore, that if the muscle is badly developed and the lower segment unyielding, pain will result when muscular effort is called for.

The anatomical findings also lend evidence in support of this view, for although we cannot state that there is any definite lesion in the uterus, we can nearly always find some departure from the normal. The uterus is generally small and may be retroverted, but is more usually anteverted with an acute anterior bend—in fact, the uterus appears to be almost curled anteriorly. Along with these conditions the cervix may be very narrow and have a long conical vaginal portion with a small external os. These conditions are congenital, and clearly point to a congenital malformation of the organ. If the external form of the uterus is malformed it is, at least, reasonable to suggest that its texture, both muscular and connective tissue, is not normal. Another fact has some bearing on this, namely, sterility, a condition which so often accompanies this form of dysmenorrhœa. Although this sterility is commonly supposed to be in some way due to the shape of the cervix, it seems much more likely that it is the result of some abnormality of the endometrium, by which the ovum finds a difficulty in becoming embedded. From all points of view then we must admit that Theilhaber's theory explains these cases best, and we may assume that the sequence of events is of this nature: The badly developed muscle allows too much blood to accumulate in the uterus, aud then in attempting to overcome this distension of the vessels the contractions are jerky and spasmodic, and soon become painful. Further, if there is any difficulty

in the capillaries rupturing owing to an unusual toughness of the endometrial connective tissue the blood will not readily escape as it should, and finally when it does escape the muscle will again act spasmodically in expelling it from the uterus.

The *congestive type* of case occurs much more commonly in married women who have had children, or in women who have been the subjects of uterine infection. It is essentially a secondary affection, that is to say, acquired years after menstruation has commenced. The character of the pain is a dull, constant aching, very severe in cases of actual recent inflammatory lesions. The pain begins before the flow, often a week before, and in a typical case is relieved by the flow. It must not be overlooked, however, that many of these patients are almost invalids from inflammatory lesions, and may have more or less constant pain, only made worse before each menstrual period.

The cause of the pain in these cases is never in doubt, and has not raised anything like the same controversy as the spasmodic type of case. The pain is due essentially to congestion, and what is more important, to congestion in an organ which is already the seat of an inflammatory lesion. It is the physiological rise of blood-pressure just before menstruation in organs already inflamed which is the true cause of the pain. The commonest actual lesion is in the uterus itself, and is a chronic endometritis, shown histologically by a thickening of the endometrium, the result of hypertrophy of glands and stroma.

This lesion is always the result of infection, such as the gonococcal or the pyogenic, following labour, abortion, or operations, or may be the result of simple, long-continued venous stasis as we see in some displacements. If, in addition to endometritis, there is also an inflammation of the Fallopian tubes, ovaries, and pelvic peritoneum, the result as regards pain is the same, only the case is a much more serious one. These three lesions—salpingitis, oöphoritis, and local peritonitis—have to be classed together because they invariably occur together, and are, as a rule, the result of an ascending infection spreading from the uterus to the tubes, ovaries, and peritoneum. Consequently these lesions are always bilateral, not always equally severe on both sides however. The occurrence of these lesions always leads to peritoneal adhesions, binding together the tubes, ovaries, uterus, rectum, intestines, and the fixed condition of these organs explain the very severe character of the pre-menstrual pain in such cases. The binding down by adhesions places these organs already under some pressure, and when the physiological pre-menstrual congestion begins these organs cannot swell up as they should, and consequently the tension in them is enormously increased. With this complexity of lesions the pain is more likely to be localised to the so-called "ovarian" regions, and even in simple endometritis the pain is often not central, but distributed to the left of the middle line over the skin area supplied by the twelfth dorsal nerve. This curious distribution is exceedingly common and very difficult of explanation, but what is of more importance than its explanation is to remember that it may occur with a perfectly normal ovary on that side. The ovaritis of the text-books is a most misleading disease, and belongs to a past age in gynæcology. True inflammation of the ovary is unknown apart from infection, and the commonest source of infection is the uterus *viâ* the Fallopian tubes. Hence ovaritis is unknown apart from salpingitis, with the exception of certain puerperal infections in which the ovary becomes inflamed by an infection following the lymphatics, and generally ends in acute abscess formation. When the ovary is bound down some of the acute pain complained of may be due to tension in a ripe Graafian follicle which is unable to rupture.

Membranous dysmenorrhœa gives rise to well-marked cases clinically, but they are comparatively rare conditions. Not every patient who passes shreds of membrane during menstruation has pain at all, and it is the character and duration of the pain plus the passage of a cast of some kind which characterises these cases. The pain commences some days before the flow and increases when the flow begins. The flow is very scanty at first, and after a day or two, in which the pain is becoming worse and worse, at last a cast is passed from the uterus, the pain is relieved and the flow becomes more profuse. The cast may be hollow, retaining the triangular shape of the fundus and having three openings, but more commonly it is a solid mass more or less retaining the shape of the uterine cavity. Whether hollow or solid these casts consist of uterine endometrium whose stroma is permeated by leucocytes and red blood-cells; in

the solid casts the endometrium is absolutely crowded and stuffed with blood-cells and the glands are much broken up. The pathology of these cases is unknown, but it is suggestive of some change in the endometrium whereby the pre-menstrual congestion takes place chiefly in the deeper layers instead of on the surface. Further, the large numbers of leucocytes exuded in the case of solid casts is suggestive of some unusually fibrous condition of the stroma which prevents blood-extravasation but allows diapedesis. The separation of the cast seems to be the result of a deep-seated blood-extravasation. Endometritis is commonly blamed for these manifestations, but it cannot be the ordinary variety, for both clinically and histologically the evidence is against it.

Whilst these types of dysmenorrhœa are on the whole characteristic, it must not be forgotten that mixed types do occur in which the symptoms are partly of the spasmodic and partly of the congestive type. This would naturally be expected, for it is quite possible for a person who has a badly developed uterus to acquire endometritis or other inflammatory lesions and consequently to show the symptoms peculiar to both conditions. This proviso in no way militates against the general usefulness of the classification.

We cannot pass on to the treatment of these conditions without a word about the combination of neurasthenia and hysteria with dysmenorrhœa. These are, unfortunately, very common combinations, and are often very potent reasons why treatment may be unsatisfactory. Neurasthenia may be acquired by a person whose menstruation is already painful, in which case the pain is made infinitely worse. It may even be induced by the years of suffering entailed by some of the congestive cases, but is rare, in my experience, as a result of the spasmodic type of pain. Again, a person who becomes neurasthenic may experience menstrual pain for the first time as a result, practically always of the congestive type. The pain in these cases is nearly always of the "ovarian" type, but does not in the least mean of necessity any real inflammatory lesion of the ovary.

Hysterical attacks may occur in some individuals only at the menstrual periods, and it is fair to assume that these nerve-storms are induced by the pain itself. As a rule such individuals show the usual hysterical stigmata, and can then be readily recognised. It is important, however, to note that hysteria rather is the result of dysmenorrhœa than the cause of it, and so the term "hysterical dysmenorrhœa" is to be deprecated. Some of the graver forms of hysteria do not show any symptoms of painful menstruation at all.

Treatment.—The successful treatment of painful menstruation is often difficult, but carried out on proper lines, each case being treated on its merits, is on the whole satisfactory. A very important point is to recognise cases in which neurasthenia plays a part, for in them local treatment of the sexual organs is almost always unsuccessful unless the neurasthenic condition can be first improved. In neurasthenic individuals seclusion is important, combined with rest, forced feeding, and massage; in fact it is in these cases that "rest" cures, and Weir-Mitchell treatment give the best results. The difficulty is to recognise the individual in whom the neurasthenia is the primary condition, as opposed to the individual who has become neurasthenic as a result of the menstrual pain. In the latter individuals operative treatment applied for inflammatory diseases of the uterus, tubes, and ovaries may bring about cures. Where, however, neurasthenia is primary operation seldom brings relief, and it is in such cases that oöphorectomy has often been done in the past without any benefit.

In otherwise healthy individuals, however, treatment is more hopeful and must be applied to each case on its merits. Congestive cases whose cause is endometritis without tubal or ovarian disease are best treated by dilatation and curettage, and are usually cured by one operation. It is, however, absolutely essential that the operation should be carried out with the most scrupulous antisepsis. It is the commonest operation performed by men who never perform any operations but the most minor surgical procedures, and the results are often disappointing, because such operators do not realise the importance of an aseptic technique. Such carelessly performed operations are not necessarily followed by serious results, although fatal sepsis has occurred sufficiently often. A mildly septic uterus, however, is easily left after a curettage and the old condition of endometritis occurs at once, and the symptoms are no better and may even be made worse. The chief point in an aseptic curettage is the preparation of the vulva and

vagina, by scrubbing each with ether soap followed by lysol solution. No amount of douching will make the vagina aseptic, for the fluid simply runs in and out without reaching the folds. Scrubbing with sterile wool swabs, however, will bring about as relatively sterile a condition of the vagina as can be produced by ordinary skin preparation before an operation. It goes without saying that instruments and swabs must be really sterile, and hands should only touch the handles of anything which actually goes into the uterus. After the operation no daily douching should be permitted, for this does no good and may be a potent source of re-infection of the uterus.

When salpingo-oöphoritis is present operative measures are usually required sooner or later for the removal of the hopelessly diseased portions of the tubes and ovaries. It need hardly be said that portions of them should be preserved if they are not hopelessly disorganised.

The palliative treatment of congestive diseases of the sexual organs resolves itself into purgation, hot vaginal douches, and vaginal suppositories of drugs, like ichthyol, which act by causing a great discharge of mucus from the cervix, and also by acting as general counter-irritants. Ichthyol suppositories should contain 10 per cent. of ichthyol in 120 gr. of cacao butter or gelatine mass. Hot douches should be copious—at least a quart, two preferably—and allowed to run as slowly as possible, so as to get a prolonged application of heat to the parts. This local treatment is not recommended for unmarried girls, for nothing is worse for the mental condition in the unmarried than some treatment which constantly calls attention to their sexual organs. It is far better in such cases to perform a curative operation under an anæsthetic.

The spasmodic cases are, it must be admitted, less satisfactory to treat, but, at the same time, operative treatment with them is often successful. Simple dilatation of the uterus, in my experience, is useless, only giving relief for one period as a rule. Such procedures as the passage of two or three Hegar's dilators without an anæsthetic are not worthy of consideration.

If the foregoing description of these cases has been followed the rational treatment is, first, thorough stretching of the uterine muscle up to 14 or 16 Hegar, followed by a thorough curettage. We cannot develop the uterine muscle in the same way that pregnancy does, but we can stretch the lower uterine segment, we can remove the endometrium, which is possibly abnormal, and we can then assist the muscle by a course of ergot in full doses. If the cervix is long and conical I always complete the operation by slitting it backwards and suturing the edges to prevent adhesion. This method absolutely cures the pain in a fair percentage of the cases, improves many others, rarely fails altogether, and in married sterile women puts them in the best condition to become pregnant. The use of a stem pessary after these operations would seem to be a possibly useful means of stimulating the uterine muscle to contract. The stem pessary, however, has the great disadvantage that it is almost always followed by infection of the endometrium with consequent endometritis. Hence up to now I have never made use of these contrivances.

We cannot, however, treat all our cases by operative means, and consequently must have recourse to drugs and general hygiene to mitigate the pain. Such drugs as antipyrin, phenacetin, aspirin, and cannabis indica can generally be relied upon to relieve pain. In my experience antipyrin is the best of them, but of course it does nothing to cure the condition, and even if it relieves pain does not produce a sense of well-being such as will permit of immediate resumption of work.

Bearing in mind the great rise of blood-pressure in the sexual organs during the pre-menstrual congestion, something may be done in picked cases by giving drugs which produce a general vaso-dilatation in the hope of diverting some of the blood from the pelvis.

Alcohol and morphia should never be prescribed for dysmenorrhœa on account of the ease with which alcoholism or morphinism may be established by the use of these drugs.

Drugs have but little effect in cases of membranous dysmenorrhœa, although the pain may be mitigated by the above-mentioned anti-spasmodics. Dilatation and curettage is the only radical means we have of influencing the condition, on the supposition that the endometrium is abnormal and must be removed.

August 9th, 1909.

DISEASES OF THE THYROID GLAND.

A Debate held under the auspices of the Hunterian Society.

Dr. ARTHUR T. DAVIES, President, in the Chair.

(*Concluded from page 272.*)

Dr. R. FORTESCUE FOX: I did not intend to intervene in the discussion; I came to learn. But I would like to ask one or two questions. I have listened with the greatest interest to these surgical contributions. In contemplating the question of operation, one naturally asks, What are the real dangers in these cases with and without surgical treatment? One has always been led to suppose that the chief danger of operation in a serious case was that of rapid death by thyroidism. I would like to ask Sir Victor Horsley if that is so. As far as I could judge he rather minimised the danger of operation. The question of diagnosis is at the root of our difficulties, and there is also the question of the *degree* of Graves' disease. One cannot help thinking that practically the presence of thyroidism is a fair diagnostic criterion. When there is obvious thyroidism, whether there is a prominent eyeball or tachycardia or not, if other evidences of thyroidism are present I hitherto diagnosed such cases as Graves' disease in the first, second, third or fourth stages. I cannot help thinking that the presence or absence of exophthalmos might easily be made too much of. There are many cases in which there is very little exophthalmos from the beginning to the end, yet in which all the other cardinal symptoms are present. I am struck by Mr. Berry's conclusion that on the whole he does not recommend operation in cases of confirmed or advanced Graves' disease. But in these other cases that he has operated upon with success there were unquestionable symptoms of thyroidism, or they would not have been diagnosed as Graves' disease. And how does he account for adenomata encapsuled in one lobe giving rise to symptoms of thyroidism? It strikes me that the various thyroid conditions really shade very much into one another. It is necessary to form an opinion in each case in what degree serious thyroidism is present, apart from any one particular symptom. With reference to prognosis and the question of operation, my own conviction is that all cases of Graves' disease, even the most serious, have a very fair chance of recovery in course of time under patient medical treatment, and that inclines me to think that Mr. Berry is right in suggesting that serious cases should seldom be subjected to the risks of operation. And for slighter cases, unless perhaps for one-sided enlargement of the gland, surgical treatment would seem to be uncalled for.

Dr. A. C. JORDAN: Very little has been said so far about electrical methods of treating this disease, and as these have been so successful I should like to say a little in this connection about electro-therapeutical and radio-therapeutical methods. They may be said to fall practically into two groups: those for treating the whole body, and those for treating the thyroid gland locally. The methods directed to treating the whole body are not cures for exophthalmic goitre, but are useful adjuncts: their action is to improve the tone and nutrition of the body, and to produce a sedative effect. I need say very little about them. Galvanic and sinusoidal currents have been mostly used, and also high frequency applications. They have a definite sedative effect, and they do a good deal in conjunction with other methods. Vibratory massage is not an electrical method but it is generally included in this category, because the small electric motors which give the sinusoidal current are used for driving the vibrator.

Local applications to the thyroid gland itself also fall into two groups: those which stimulate the thyroid gland, and those which diminish its secretory activity. Of those which stimulate, the galvanic treatment is the one which has been used for the greatest number of years. It is the earliest of the methods, and it is still, on the whole, the most popular. The sinusoidal treatment of the thyroid gland is practically the same as regards its results. As to the results of galvanic treatment, there are very few cases in which a good start is not made with it, that is to say, a considerable amount of very definite improvement in the cardinal symptoms occurs quickly and goes on steadily, and ends in what must be termed a cure. But in some cases a disappointing thing is apt to happen. The treatment begins very well, but after

a certain length of treatment no further benefit is obtained. For instance, during almost the first week things begin to improve: the tremors begin to get less, the patient becomes quieter, and she very soon begins to gain weight. This goes on for a month or two months. At the end of that time, that is to say, during the third month, the improvement is very slight, and afterwards one seems to come to a standstill with the treatment. This is very disappointing after so promising a start.

It is in these cases that there are two special forms of local application which have been found very useful in carrying on the improvement which has been so well commenced by galvanic treatment. These are—first the so-called static wave discharge which was described by Dr. Benham Snow, of New York. A static machine, such as a Wimshurst, is used. The patient is placed upon an insulating stool; one terminal is connected to a moulded electrode on the thyroid, and the other is earthed. A parallel spark-gap is used; at the beginning of the application this is adjusted so that the brass balls are almost in contact. They are then gradually separated, when a regular series of sparks passes between them. At each discharge the potential of the electrode on the thyroid gland falls suddenly, sending a "pulse" through the gland. The balls should not be separated so far as to cause the muscles of the neck to contract.

The other method is one I have myself described, though I lay no claim to originality. A Faradic coil is used, the primary of the coil being connected to the electrodes. The best coil for the purpose is one wound with a primary only, such as is made for alternating current applications in a bath. A Wagner's hammer, which can be adjusted to give regular slow interruptions, is used, and across the interrupter terminals is placed a condenser of some capacity—$\frac{1}{4}$ microfarad. The patient receives a series of pulses which are by no means unpleasant. The discharges are entirely at break, there being practically no discharge at make. When progress with galvanic treatment has come to a standstill this method often enables one to continue the improvement many stages further.

We now come to the important methods of diminishing the functional activity of the thyroid gland, viz. electrolysis and X-ray treatment. I have no personal experience of the former. The method first described was to use a steel needle which was made the positive pole, the result being the deposition of a little oxide of iron in the gland; this is followed later by leucocytosis and fibrous tissue formation. It is more usual to make the needle the negative pole, and thus to obtain the deposition in the gland of caustic soda, the final results of which are similar, while hæmorrhage is easily checked by the coagulating action of the caustic soda. The result of electrolysis is the same as that of electrolysis upon large nævi. It is said that the amount of thyroid gland which is thus put out of action can be exactly regulated, so that the result is practically the same as that of the partial surgical extirpation of the gland. A point of some practical importance is that the needle should be insulated with varnish, excepting at its point, so as to prevent destruction of the skin and subsequent unsightly scarring.

The X-ray treatment of exophthalmic goitre was introduced with a great flourish, and in the early days some cases ended in disaster, acute dermatitis being set up. As the result of this the treatment rather got into disfavour for a time, but at the present time dermatitis should never be produced. With care in the selection of suitable tubes and in regulating the duration of the treatment, etc., it is quite easy to avoid any risk of producing dermatitis. It is important to protect the skin from the most readily absorbed rays by the use of a suitable filter such as a thick layer of felt. In some of the earlier cases myxodema was produced, and in these cases the result of the treatment was the same as that of total extirpation of the thyroid gland. It is now usual to expose only a part of the thyroid gland, or in cases with severe toxic symptoms to commence by exposing the whole of it, and as soon as the symptoms of hyperthyroidism are passing off, to continue the treatment by exposing a part only of the gland. The treatment must be continued for many months. The surgical removal of part of the gland is frequently followed by success, but in other cases no benefit follows, and in these latter cases the remaining portion of the gland has been exposed to X-ray treatment with great benefit. With regard to the results of X-ray treatment these must be considered from the point of view of the effects upon the cardinal symptoms of the disease.

In almost every case there is a sedative effect which is manifested very early in the treatment.

In 90 per cent. of the cases the rate of the heart-beat diminishes, and the palpitation is relieved. In two thirds there is a gain in weight, and this frequently commences early and is great in amount.

With regard to the goitre the results are less uniform. At first it occasionally becomes rather more tense, but gradually it softens, and in quite 20 per cent. of the cases it diminishes materially in size.

The exophthalmos is the most obstinate symptom. It is the last to yield to treatment, and in many cases it persists. Many patients are discharged feeling perfectly well, and free from all their symptoms, but they still have prominent eyeballs. This may throw some light on Mr. Berry's difficulty in appreciating the difference between a cure and a perfect cure. Such a patient considers himself cured though he is still exophthalmic.

In these days one cannot speak of X-ray treatment without the thought of radium immediately presenting itself, and I had hoped to say something about radium. As the hour is late, however, I propose to reserve what I have to say on this subject in case there may be an opportunity later in the evening.

Dr. W. H. KELSON: I have listened to the speeches with very great interest, but with a little disappointment as to the practical application. One cannot help feeling that when a patient comes it is necessary to have some sort of definite point in one's mind when deciding whether to advise that patient to have the goitre operated upon or not. And in the ordinary way I think the average surgeon would say that with the ordinary case of enlarged thyroid there is no danger practically at all in operating; whereas, apart from whatever the results may be in the hands of a few experts, in the case of exophthalmic goitre there is, generally speaking, considerable danger to life. Sir Victor Horsley, in illustrating what he meant by exophthalmic goitre, showed some slides of microscopical sections on the sheet, and one would rather draw the logical conclusion that if one wants to make a definite diagnosis of exophthalmic goitre one should remove a small piece of the thyroid and examine it microscopically, if that is to be the only way in which one can definitely say whether a thyroid belongs to that class or the other, I should like to hear from Mr. Berry what points of difference he makes between the two in difficult cases. He said he called no case exophthalmic goitre unless exophthalmos was present. Does he make that prominence of the eyeball, the rapid pulse and the enlargement of the thyroid the things which cause him to diagnose exophthalmic goitre. and therefore decide that that patient must not be operated upon?

Mr. T. H. OPENSHAW: We are all indebted, sir, to Mr. Berry and Sir Victor Horsley for their very interesting papers on the surgical aspect of the thyroid and exophthalmic goitre. I learn with regret that Mr. Berry, whom we have for years recognised as the authority on the surgical treatment of goitre and exophthalmos, should ultimately have the opinion that only cases should be diagnosed as exophthalmic goitre which were in such an extreme condition as practically to be inoperable. A patient may have slight enlargement of thyroid and a rapid pulse and tremor, and little or no exophthalmos. Some people diagnose such a case as exophthalmic goitre and others may not. I presume Mr. Berry would operate upon cases which most people would diagnose as exophthalmic goitre. Very slowly during the past twenty years the cases which I have operated upon for enlargement of the thyroid have extended until at the present time I scarcely hesitate to remove any thyroid. The other day I had a case sent to me by Dr. Houchin, of Ilford, a girl in a family of three, two of whom had died of exophthalmic goitre. She had an enlarged thyroid and prominent eyeballs, with palpitation and tremor. Although she was not a very pronounced case yet she was a definite case of what I am in the habit of diagnosing as exophthalmic goitre. The doctor said she was getting rapidly worse. I operated, with a perfect recovery. For my own part I would say that there is no case of what is usually called exophthalmic goitre, where the patient was definitely getting worse in spite of medical treatment, in which I would not entertain the desirability of removing some portions of the thyroid gland. I was very pleased to hear Sir Victor Horsley say he considered that the anæsthetic had more to do with a grave issue than the operation. I am quite in accord with this opinion. If the operation is

done carefully and slowly, and all the bleeding checked as it occurs, so that the operator can go on slowly and calmly with the work, the operation is, even in severe cases of enlargement of thyroids, a safe procedure. I should like to tender my thanks to Sir Victor Horsley and Mr. Berry for the excellent papers they have given us.

Dr. W. Langdon Brown: I think we have almost reached this point in the discussion: that the only way you can distinguish between goitres with toxæmic symptoms and Graves' disease is by the microscopical method, and that it is necessary to remove a portion of the gland before you can be sure, as there seems no substantial agreement amongst authorities as to what constitutes Graves' disease clinically. And in view of the fact that many authorities are very much opposed to operating in the severer cases, it seems an unfortunate position of affairs that we should have to do this to people who are unsuitable for operation. Sir Victor Horsley brought out quite clearly the fact that Graves' disease must be regarded not merely as hyper-thyroidism, but rather as a perverted condition of secretion, so that it may even be combined with myxœdema. I remember seeing in one case there was combined with the exophthalmos an enlarged thyroid and tachycardia with a mitral murmur, and a marked condition of myxœdema of the skin. That case was under the care of Dr. West at St. Bartholomew's. Very little has been said about the thymus in this condition. In a typical case of severe Graves' disease with morbus cordis under my care, which proved fatal, I found not only the appearance which Sir Victor Horsley has described as typical of Graves' disease, but a persistent thymus, which is known to exist nearly always in Graves' disease. In this thymus the most striking feature was the enormous size of Hassall's corpuscles, nearly the whole field of the microscope being filled by enormous concentric corpuscles. I have not found that condition described in the literature, and I should like to hear from the authorities to-night if they know of it being recorded that you meet with those large concentric corpuscles of Hassall in the thymus in Graves' disease. The persistent thymus is further interesting because Graves' disease comes on at a time of life when it should have atrophied. Are people predestined to Graves' disease, or why is it that there is this persistence at a time when in the ordinary course it should have atrophied? With regard to the medical means of treatment, speakers at the previous meeting referred to rodagen and thyrodectin, both of which I have found to lead to some improvement. No one referred, however, to thyrolytic serum. Professor Murray made a communication on that subject some years ago. He thought that by feeding an animal with thyroid or injecting people with thyroid juice you get a thyrolytic serum. I suggest that that would not be a rational way of treating Graves' disease. In the first place, cytolytic sera are fairly specific for the animal for which they are prepared. If you feed an animal on goat's thyroid it might develop a serum which would be thyrolytic for the goat but not for human beings. Cytolytic sera are only specific for the particular animal, but they are not specific for a particular gland—that is to say, in cats injected with thyrolytic serum prepared in this way not only are some of their thyroid cells destroyed but some of their liver-cells are destroyed also. So you are faced with this fact: either thyrolytic serum would be ineffective, or if it were effective it would be dangerous. For if in trying to cure Graves' disease you produced an acute atrophy of the liver, it is evident that the patient would not be much beholden to the treatment.

Sir Victor Horsley, in reply, said: It has been a very interesting discussion, Sir, and I think the questions which have been put to Mr. Berry and myself have been extremely fair ones, because they amount practically to this: What is your means of differentiation? You have described certainly two classes of cases, which we may call "pseudo-exophthalmic goitre" and "real exophthalmic goitre." How do you tell the difference? I always agree with Mr. Berry in most things, and I believe I shall be quoting him correctly when I say that as far as I am concerned the first thing I rely on is the physical examination of the thyroid gland. What he and I call "pseudo-exophthalmic goitre," or what I called just now "parenchymatous goitre" with toxæmic symptoms, I can detect from physical examination of the thyroid gland alone. Parenchymatous goitre can be felt as such, and it has a different feel from that of true exophthalmic goitre such as I threw on the screen. And personally I am inclined to quote that as the first method of

differentiation. I do not think it would be necessary—although I appreciate the point—to remove any portion for microscopical examination. I fancy that the better diagnosis by palpation nowadays is the reason why, as Mr. Openshaw pointed out truly, we are operating more and more on the thyroid gland. And as regards the question of true exophthalmic goitre, Mr. Berry and I are in absolute accord as to the class of case which we neither of us would operate upon, which I call the desperate case, in which the fall in metabolism is so great that the patient's emaciation reveals to you the fact that he is on the brink of a precipice. In regard to the point which was mentioned concerning the danger, I was asked whether I thought it was hyperthyroidism. No, I do not think it is. It is an aberrant thyroidism, for the secretion is altered. It is not hyper-secretion, but aberrant secretion. I do not think the patients who succumb have succumbed from absorbing thyroid juice from the remainder of the gland which is left. I think that any traumatism would in such cases bring about a fatal result: if they had broken their leg they would probably die from the restlessness and tachycardia which Mr. Berry has described. The question was also asked how was it that an adenoma buried in the thyroid gland could cause toxæmic symptoms? I endeavoured to show some years ago that every adenoma of the thyroid gland caused toxic symptoms, and perhaps the most interesting effect of adenoma is the effect on the metabolism, because as I said with exophthalmic goitre it is the change in the metabolism which is the threatening element in every thyroid case. In the case of an adenoma, if you take the trouble to weigh the patient and test his motor power before you operate, you will find that six weeks after the operation he has gone up on both those points, especially in regard to weight, in other words his metabolism is improved. I think nobody can have an adenoma of the thyroid without a certain amount of toxæmic symptoms. It is a question of degree. I was extremely interested to hear Dr. Jordan's observations on the difference between galvanism and faradism. When I was a student we were taught that the galvanic current was the only means of influencing the thyroid gland. A very short experience showed that faradism was far better, and I have written frequently on that subject, but apparently, as he said, the galvanic current is still the more popular even at the present day. With regard to X rays and the question of "cure" or "perfect cure," I have at present coming up to London a lady who is greatly benefited by partial removal of the thyroid, and whose final cure I hope to see obtained by the radiographer. I thank you once more for your kind opportunity of discussing this question.

Mr. JAMES BERRY: Most of the questions addressed to me by speakers have already been answered by Sir Victor Horsley, and I am in substantial accord with what he has said. I would add as a practical point that when a patient has unilateral enlargement of the thyroid it is exceedingly unlikely that this will be a case of genuine exophthalmic goitre; in fact, it is impossible that it could have been a genuine uncomplicated case of Graves' disease. It might be a case of old cyst or old adenoma to which the other symptoms had been superadded. Most of the cases to which I have referred as false or secondary Graves' disease are cases of a single adenoma or cyst. Such cases are nearly always capable of cure by operation, whatever the symptoms are.

These cases seldom have exophthalmos. I admit that it may be very difficult, and even occasionally impossible, to say definitely whether certain cases are examples of true Graves' disease or not. In the vast majority, however, of the cases of Graves' disease that come under our notice in actual practice there is no question about the diagnosis; it is self-evident to anyone who has had the smallest experience of the subject.

The CHAIRMAN summed up the discussion, and the thanks of the meeting were tendered to Sir Victor Horsley and Mr. James Berry for their addresses. Mr. Openshaw was then presented with the Hunterian Medal as an emblem of his presidency for the ensuing year.

August 9th, 1909.

E. FRANK reports the case of a woman, æt. 26 years, who, six days after a severe fright, developed a hemiplegia without loss of consciousness but associated with headache. After six weeks movement returned in one finger and gradually the patient improved. Though there were many hysterical symptoms there were definite signs of an organic lesion.—*Med. Record*, vol. lxxvi, No. 4.

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SOME ELEMENTS OF THE THEORY OF IMMUNITY.

By E. VON OFENHEIM, M.D.

ONE is frequently asked by gentlemen in general practice to give the rough outlines and principles of immunity in a short and concise form without many details, and, so to speak, in a nutshell. This is rather difficult, the science of immunity being such a complex one that it would require volumes to give only a faint idea of the almost unlimited powers and wonderful actions of the animal blood on micro-organisms and organic substances, and *vice-versâ*. In this paper an attempt is made to bring forth only those parts of the science of immunity which are of interest from the medical point of view, and which are of hygienic and therapeutic importance. It claims in no way to be complete or to exhaust the subject in any direction.

To give an exact definition of immunity is almost impossible, as there is such a large number of phenomena which have to be classified under this name, which is almost daily increased, so that the original idea of immunity has been completely altered and is taking a different shape in almost every single instance. Therefore one must not apply the rules of logic too strictly if immunity is described as *the expression of the resistance of the animal organism against the action of other organisms, respectively organic substances.*

It may perhaps appear to be beginning at the wrong end if we first try to make a classification of the various kinds of immunity before going into the theory of it, but the latter will probably be easier to understand if one first has a general idea as to the various kinds of immunity with which we have to deal. The table given below does not claim by any means to be complete, but is only a skeleton of which the ligaments, muscles, and other structures have been stripped off.

"Immunity" is perhaps not a very appropriate expression, and ought to be replaced by "resistive power," as we shall see presently, but it has been adhered to in this paper as it is a more common expression and will make matters more familiar.

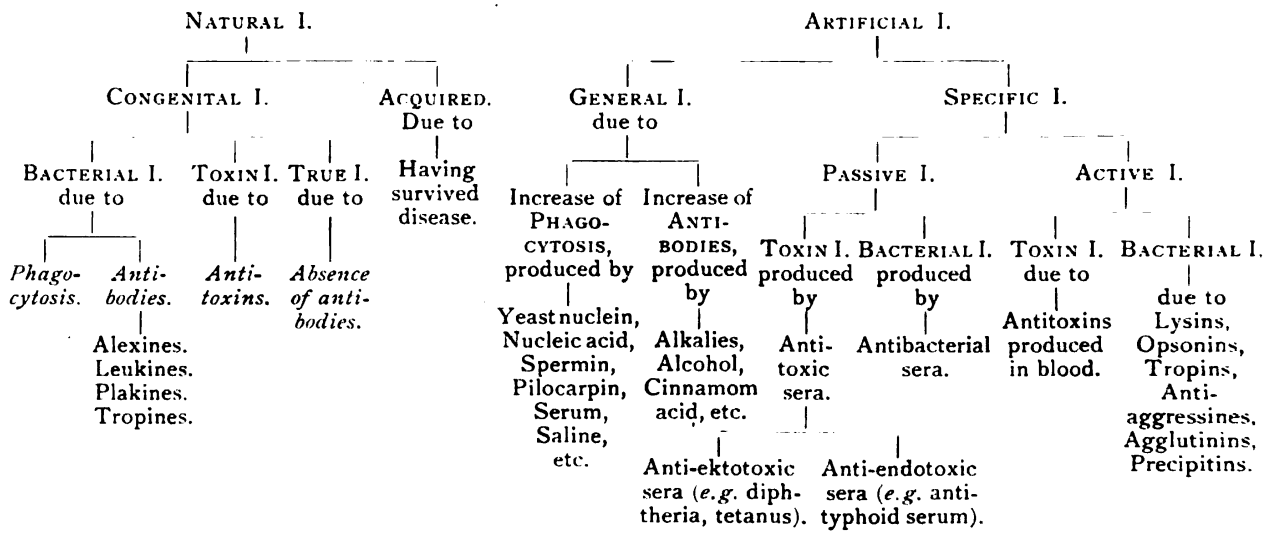
First of all we must split up the immunity into natural and artificial immunity—that means to say an immunity which is produced without any interference, and an immunity which is produced by artificial means which are the outcome of the experience and assiduous research of centuries.

The natural immunity again must be divided up into a congenital one and an acquired one. The congenital immunity may be either bacterial —that means an immunity against the infection of the system by bacteria, or a toxin immunity which is a resistance against organic poisons. The former can be either caused by phagocytosis, as Metschnikoff has shown, or by anti-bodies, *i. e.* substances in the blood-serum which have the property of killing off micro-organisms, and which are present for certain bacteria and to a certain extent in all animal blood. Of these only the alexins of Buchner, the leukines, plakines, and tropines out of many others shall be quoted. It would take too long to go into details of all these substances, and it should only be mentioned that the origin of the alexins is not fully known yet; Metschnikoff believed they were only products of destroyed phagocytes—a theory which is no longer accepted. The leukines are products of the phagocytes, not only of the dead ones, but also of the living ones, as Schneider has proved. Plakines are the substances which Gruber and Futaki have succeeded to produce from blood-platelets. The origin of tropines is not yet known, and it is perhaps not quite correct to put them under this heading, as they have no bactericidal power of their own, but act in combination with the phagocytes in such a way that they prepare the micro-organisms for phagocytosis.

Under toxin immunity we understand the resistive power of the serum of certain animals against poisonous products, but *not against the originators of these products themselves*. The toxin immunity is due to the power of the serum of certain animals to produce antitoxins very quickly, and to such an extent that the pernicious action of the toxin is annihilated.

There is the third class of congenital immunity, which is perhaps the only one to which the name of "immunity" *sensu strictiori* applies. This is the immunity which applies in some cases to bacteria, in others to toxins, and which is due to the complete absence of the formation of anti-bodies. This will be clearer later on when Ehrlich's theory is explained. For instance, if we inject large quantities of tetanus toxin into an alligator or a chicken it does not affect them in the least; but this toxin is not annihilated in the way it is by some animals, by the formation of anti-bodies, but circulates freely in the blood-stream of the animal, and if the blood of this animal, which is keeping quite well in itself, is injected into

TABLE I.—*Immunity.*



another animal which is susceptible to tetanus toxin—for instance, a guinea-pig—even after some months' time, it produces all the symptoms of tetanus poisoning.

The natural acquired immunity is the consequence of an animal or human being having survived certain diseases, and it is an every-day experience that a man having had smallpox, whooping-cough, plague, typhoid, etc., is immune against these infections for a time, if not for ever. This experience is really the origin of all immunisation work, and was the leading idea of Jenner when he first introduced smallpox vaccination some 200 years ago. Of course it is well known that not all bacterial infections produce such an acquired immunity, and that some of them even, on the contrary, make the organisms more susceptible to new infections by the same organisms. Many patients who have survived an attack of influenza, pneumonia, etc., are more liable to fresh attacks than others. This is not by any means contradictory to the previous statement, and there are several explanations for it, but it would not be within the limits of this paper to go into the details of the matter, although it shall be referred to again later on.

More interesting than the natural immunity, from the practical point of view, is the artificial immunity. In classifying the artificial immunity we have first of all to split it up into general and specific immunity.

General immunity comprises a certain amount of resistive power against various kinds of organisms and poisons. It is that condition which is commonly called "strong health," a condition which can be brought about by improving the diet, surroundings, way of living, exercise, rest, etc., and which can be diminished by alcoholism, various excesses, unreasonable way of living, overwork, constitutional diseases as gout, diabetes, etc. If we investigate the causes of this general immunity, we find it is again produced by an increase in the number of phagocytes, or by an increase of the natural anti-bodies which have been mentioned under the heading of "natural bacterial immunity." Phagocytosis cannot only be increased by general means, but also, as experiment has shown, by the action of certain chemical substances, as, for instance, yeast nuclein, nucleic acid, spermin, pilocarpin, normal serum, and even ordinary saline. On the other hand phagocytes can be destroyed by chronic alcoholism, or other poisons, especially also by quinine, as it is known that the action of quinine to lower the temperature is chiefly due to destruction of leucocytes. From this it is easily understood that quinine is contra-indicated in all bacterial infections. It is a different matter, of course, in plasmodic infections, as, for instance, malaria, in which the leucocytes are practically of no importance, and where the quinine acts direct on the organisms. From this short explanation one can also gather that the leucocytic count, on which great stress has been, and is still, laid in diagnosis, is of a very questionable and limited value. There are many factors which are able to increase or decrease leucocytosis in the normal system, and the number of leucocytes fluctuates considerably even in the same individual at various times.

An increase of anti-bodies in general can be produced by alkalies, cinnamomic sodium (Miller), alcohol in sudden large doses (Friedberger, Fraenkel), contrary to the decrease of resistance due to chronic alcoholism, etc. Exercise also, by which a general hyperæmia of the peripheral circulatory system is produced, as well as the localised hyperæmia and permeation of the tissues with serum, as, for instance, by Bier's passive congestion, increases the anti-bodies in the serum.

The value of this general artificial immunity is a very small one, and no doubt very limited. We have very little, if any, possibility of controlling or measuring it. There is no standard for it, and any description of it passes off very quickly. Most of the substances mentioned act on the blood-producing organs, and this is probably the only way by which they act at all.

Of much greater value is the specific artificial immunity; that means the immunity against special kinds of organisms and poisons, which we can produce at our will, which we can control, and the presence or absence of which can be clearly shown experimentally.

There are two distinctly different kinds of specific immunity—the so-called "passive immunity" and the "active immunity."

Under passive immunity we understand the resistance which is produced in the body by substances which have not been prepared by this body itself, but by protective substances which have been

developed in animals as the consequence of an introduction of the actual poison or organism, as the case may be. No active part has to be played by the individual on which immunity has been conferred in this way. Of course, here, also, we have a toxin immunity and a bacterial immunity, according to whether a resistive power is produced against the toxin or against an infection of organisms. We call the serum which is used for this passive immunisation against toxins "antitoxic serum," and this is probably the best known and widest-used kind of all immunisation at present. Every medical man is nowadays quite familiar with the diphtheria antitoxin of Behring, which goes under this heading—"the tetanus antitoxin" (Behring, Roux, Vaillard), etc. These antitoxins are produced by injecting animals, chiefly horses, with the toxin against which we want to immunise, not with the organisms which are producing this toxin. When an immunity against the toxin has been produced in the animal, the serum of that animal is drawn off and contains a strongly antitoxic substance, which, of course, injected into anyone who has toxins in his blood, acts with a curative effect. It would lead too far into technical questions to explain here the most elaborate and accurate methods by which the strength of these antitoxic sera can be tested and standarised. On the other hand, it must be well understood that these antitoxic sera have *no influence whatever on the organisms which are producing the toxins, but only on the toxins.* This at once explains the advantages, disadvantages, and conditions under which we can use and make such antitoxins. The first condition, of course, is that there should be a toxin given off from the organisms into the blood of the patient, and which is not adherent to the organisms themselves. This is the case with diphtheria and with tetanus, where the organisms remain on the infected part, sending their poisonous substances into the system, by which they are killing their victim.

Lately an attempt as been made by MacFadyen to produce anti-endotoxins also—that means antitoxins which counteract and neutralise those toxins of bacteria which are adherent to their bodies and are not given off into the blood-stream. Hewlett has quite recently taken up this idea again, and although the time since experiments in this direction have been started is too short, and the experience with them is not yet wide enough to permit a conclusive opinion, it appears that very good results have been obtained, especially in the treatment of typhoid fever, with these anti-endotoxic sera.

The advantages of the serum treatment are that we bring into the system protective substances ready made, that there is no effort on the part of the system of the patient, that no time is lost, but that immunity begins almost instantly after the antitoxins have been brought into the blood-stream.

The disadvantages are that this immunity lasts but a very short time, and that it does not affect the bacteria, the originators of the toxin.

The bacteria themselves in these cases are, as a rule, destroyed by bacterio-lysins, which, of course take some time to develop, and thus time is gained by protecting meanwhile the system against the toxic effects of the bacteria by the antitoxic treatment.

Another drawback to the treatment with animal serum is that if this treatment has to be prolonged or repeated within a certain time, a hyper-sensibility against the serum is produced, and one has an opportunity of observing what Pirquet and Schick have called the "serum illness." In slighter degrees one frequently sees a serum rash, and pains in the joints appear from a week to a fortnight after the injection of any kind of antitoxin. These pass off very quickly and without serious consequences whatever, but if these serum injections are repeated, especially at intervals, one might get most serious and alarming symptoms. These are not due to the antitoxins, but due to the serum, which acts apparently on the serum of another animal species, to a certain degree poisonous.

But not only for bacterial poisons antitoxins can be produced in the blood; we know that the blood reacts by the productions of antitoxins to a good many other organic poisons, as, for instance, the snake poison, poisons of the scorpion, several poisons of the vegetable world, as, for instance, the ricin, the abrin, and others.

As successful as science has been in conferring passive immunity for toxins, so unsuccessful and poor have been the attempts to confer passive bacterial immunity. I expect that practically every medical man nowadays has heard, and perhaps even tried, anti-streptococcic serum, anti-staphylococcic serum, anti-tubercular serum, etc. It stands to reason that these sera are not anti-

toxic, as the organisms mentioned do not give up ektotoxins—free poisons—into the system, but they kill by themselves, by their own presence, respectively by the endo-toxin—that is, those poisons which are attached to their own bodies. The blood reacts to infections with these pyogenic organisms chiefly by the production of tropines or opsonins, which, being very unstable and soon destroyed if kept only for a few days, can practically not be transferred in the way in which antitoxins can be.

Besides the theoretical explanation, it is technically very difficult, if at all possible, to standardise these anti-bacterial sera. Doubtless some have had in their experience cases which apparently derived benefit from the injection of these so-called anti-bacterial sera, but this benefit is not as a rule, due to any specific substance in the sera, but is simply due to the amount of alexins, respectively tropines, which are contained in any animal serum and which one can get just in the same way if one simply uses normal horse-serum, or better still, human serum, *provided it is quite fresh.* The latter is not easily to be got; the former is already used to a great extent, but, unfortunately, only applies to a very small proportion of cases, owing to the fact that the alexins and all the anti-bodies in the horse do not exactly correspond to the anti-bodies in the human system.

According to Wright, in a number of cases these sera also might act as a vaccine, as they contain a certain amount of endotoxins which have been washed out from the organisms and remain in the serum, but, of course, the amount of these endotoxins cannot be measured, besides the difficulty that every species of bacteria produces its own anti-bodies. It has, therefore, been tried by Denys, Van de Velde, Tavel, Aronson and others, to produce sera from a large number of species, but, of course, it is impossible to get them all, and therefore it is a mere stroke of luck if that particular species which is causing the disease in the patient should be amongst the species which have been used to prepare these sera. These sera, which have been obtained by having inoculated one animal with strains of various species of organisms, are called *multipartial* sera. Experience has shown that the efficiency of the serum is to a great extent dependent also on the species of the animal which is used for its production, and that, for instance, for certain kinds of bacteria the immune serum derived from a horse is useless for man, whilst the serum obtained from sheep which have been immunised against these micro-organisms confers to a certain extent a passive immunity to human beings. For other microbes, again, the horse immune serum has some value and that of sheep has none, and so on. To overcome this difficulty the serum of various kinds of animals which have all been immunised with the same species of bacteria, have been mixed together, and the serum obtained thus is called a *polyvalent* serum.

As to the active specific immunity, this is produced by the wonderful power of the blood to react to every infection or introduction of toxins by special anti-bodies which are specific for that particular infection or poison. Accordingly we have also to divide the active specific immunity up into a toxin immunity and a bacterial immunity. The toxin immunity is produced by the introduction of toxins, and a man can be immunised against various bacterial and other poisons by introducing into his system small doses of the actual poison in a gradually increasing amount. This is what Behring terms the "mithridatic immunisation."

In practice this way of immunisation is of very little value, because we cannot possibly immunise ourselves against all the possible poisons to which we may be exposed. On the other hand, when the disease is established, or when the poisoning has already taken place, it is too late to use this method, because there is already a considerable amount of toxin in us, and it would not only be useless but even dangerous to increase that amount, and in this case we have to take our refuge in the passive method of immunisation by the ready antitoxin. One must not confound this kind of getting used to a poison with the way by which the alcoholic or the morphia maniac gets accustomed to his poisons. This is an entirely different action. The alcohol, morphia, cocaine and other alkaloids are not neutralised in our body by the production of anti-bodies, but are eliminated in various ways by the urinary system, by the bowels, etc., this elimination taking place quicker and quicker, which is the reason why in morphia mania, alcoholism, cocainism, etc., doses of these poisons can be consumed with apparently no harm which would be fatal to an individual who is not accus-

tomed to them, only leaving their marks by the gradual destruction of certain tissues.

Specific active bacterial immunity is due to various anti-bodies which are produced in the blood by the contact of the blood itself with these bacteria. These anti-bodies vary a good deal, not only in their chemistry but in their origin, and in the way in which they act. The principal ones of them are enumerated in Table I—the lysins, opsonins, tropins, anti-aggressins, agglutinins, and precipitins.

The lysins are substances which have the power of, so to say, dissolving bacteria, so that they are split up and killed. We meet these substances, for instance, in cholera, typhoid, etc., and if cholera vibrios, or typhoid bacilli, are injected into the peritoneal cavity of a guinea-pig or rabbit, and some serum is injected at the same time containing specific lysins for these organisms, the animal will remain healthy, and the fluid drawn off after twenty-four hours will only show fragments of the bacteria. The blood is able to produce such lysins not only in response to bacterial injections but also in response to several other substances, as, for instance, blood-corpuscles. If we call the former "bacterio-lysins," we call the latter "hæmo-lysins." Other cells also can produce this phenomenon, and then we speak of "cyto-lysins." These are only mentioned as they also form part of immunity.

As to the opsonins and tropins, these are substances which have not actually bactericidal power, but which, as stated before, prepare the bacteria in such a way that they can be taken up and digested by the phagocytes, so that we have here a combination of phagocytic and serum immunity.

The anti-aggressins, again, are anti-bodies which are produced in response to aggressins. These latter are bacterial products which appear after a long struggle has been going on between the organisms and the blood of the infected individual. When the bacteria are pressed hard in their fight against the various anti-bodies—artificial or natural ones—they produce, as a last attempt at self-defence, aggressins, substances which protect them not only against the most ferocious of all phagocytes, but also against those anti-bodies to which they would have fallen a victim under ordinary circumstances. But so wonderful is the multiplicity of the blood powers that after a time also, against these, and in response to their presence in the system, other anti-bodies are formed, which have been called anti-aggressins.

The agglutinins, which are familiar from Widal's reaction, act, as their name implies, by glueing up bacteria into clumps, and in this way depriving them of their activity. It was mentioned earlier that typhoid was counteracted by lysins, which seems to be a contradiction of the fact that typhoid patients get a high agglutinating power as well, but this is not the case. Lysins are produced at the first onset of the disease whilst agglutinins only put in their appearance much later, and sometimes not at all, and this is the explanation why the agglutination test rarely comes off before the second week of the disease, and very frequently does not come off at all. The lysins, on the other hand, are very unstable and disappear very soon, whilst the agglutinins remain in the blood for many years, as Eyre and others have proved.

The precipitins act in a similar way to the agglutinins only with the difference that they do not form clumps of bacteria, but clumps of an albuminous substance, which has been introduced into the system in some way or another. For instance, if human serum is injected into a rabbit, and the serum of this, as we then call it—"humanised rabbit"—is brought into contact with human serum, the liquid becomes opaque, and a precipitate falls out owing to the precipitins of the serum. This is a very interesting fact as it can be used for various examinations and tests, the most important of which is perhaps the differentiation between human and animal blood for forensic purposes (Uhlenhuth, Wassermann and Schultze). There are methods in this way by which even dilutions of 1 in 1,000,000,000 of human blood can be detected (Friedberger).

It is clear that the bacterial immunity is of the greatest importance, and has probably the greatest future of all. It gives us the possibility of immunising against various infections, and to immunise for some considerable time. On the other hand we have the possibility of a curative immunisation when the disease already exists, as we can increase the anti-bodies to a particular organism by bringing into the system dead or mitigated cultures of that organism, and in this way give the blood an impulse to stronger and

quicker formation of anti-bodies without endangering the patient. The dosage of these *vaccines* can be measured most accurately, and by various methods an accurate estimation of the action of the administered dose on the blood of the patient is obtainable. The presence of every one of the anti-bodies enumerated under this heading cannot only be found in quality but also in quantity by laboratory experiment.

TABLE II.—*Theory of Bacterial Immunity.*

PHAGOCYTOSIS *only*.	SERUM *only*.
(Metschnikoff, A. O.)	(Koch, Behring, Pfeiffer, A. O.)

SERUM + PHAGOCYTOSIS.

(Wright, Douglas, Denys, Marke, Lecleffe, Gruber, Futaki, Neufeld, Rimpau.)

In the second table (II) it was tried to make clear the three principal theories on which bacterial immunity is based.

Metschnikoff and his school have put their trust in phagocytosis only. Koch, Behring, Pfeiffer, Ehrlich, etc., expect their salvation from the serum and its contents, whilst Wright, Douglas, Denys, Marke, Lecleffe, Futaki, Gruber, Neufeld, Rimpau, and others have found that serum and phagocytes must work together with the anti-bodies in the serum which have to prepare the bacteria before they can be eaten up by the phagocytes. Which theory is the right one? As in so many cases we must say that all three theories are correct. There can be no doubt that certain organisms of no, or very low, virulence can be swallowed up by the phagocytes without any other help. On the other hand it can be proved under the microscope that the phagocytes absolutely refuse to take up other organisms if they have not come into contact with the serum containing certain anti-bodies. Again there are a great number of bacteria which are killed and annihilated by the serum alone, without the presence of any phagocytes at all, as can easily be shown *in vitro*.

As in science in general, and in medicine in particular, it is always a mistake to generalise, so it is in immunity. It is the purpose and the aim of the immuniser's work to find out to which species of organisms the one, and to which the other theory applies. We cannot shoot elephants with a rabbit gun, or quails with a big game rifle.

So much for the classification of the various kinds of immunity.

After having gained a general idea of the multiplicity of blood powers, it will be an easier and shorter matter to give a superficial account of the main points of the theory.

In spite of many attacks which have lately been made on Ehrlich and his theory, his explanation of the phenomena we meet with in immunity still holds good, and is the only one by which, so far, we are able to explain practically all our observations. It would be impossible in a short paper to deal with all the details of Ehrlich's *side-chain* theory, and in order to give the nucleus of it in a few words, it will be best to represent it graphically.

In Figs. 1 and 2 the action of antitoxins is

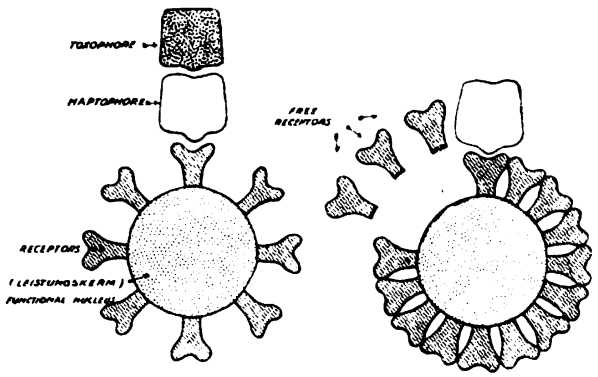


FIG. 1. FIG. 2.

demonstrated. Ehrlich assumes that every cell has what he terms "receptors," that is, speaking symbolically only, of course, anchors by which poisons can be attached to the cell and can get an influence, respectively a poisonous effect on them. In diagram No. 1 a number of these receptors are shown as an animal cell might have them; of course in reality they are neither visible nor of any known shape.

The toxins consist, according to Ehrlich, of two different groups, each molecule of toxin containing a haptophore and a toxophore group. The haptophore group is the one which clings to the receptors of the cells, whilst the toxophore group can only get into contact with the cell by means of the haptophores. On the other hand the attachment of the haptophores to the cells alone does not produce any toxic symptoms; destruction or poisoning of the cell only takes place after the

toxophore group has been added. The time which elapses from the moment of the infection until the moment the toxophore group is attached to the haptophores is what we call the "incubation period." This incubation period varies a good deal, not only according to the kind of toxin, but also according to the species of animal, and depends a great deal on other circumstances, as, for instance, temperature, general immunity, etc. For example, if we inject tetanus toxin into a frog and keep this frog at 10° or lower of the centigrade scale, this animal will not show any symptoms of tetanus poisoning; but if we put it into water at a temperature of 37° C. (98·4° F.), all the clinical symptoms of tetanus will soon develop. If, now, at the same time as the toxin, a sufficient amount of antitoxin is injected, no symptoms will appear and the frog will remain healthy; but if we first inject the toxin and the antitoxin only some time later, and then bring the frog into a temperature of 37° C., in spite of the antitoxin the frog will develop all the symptoms of tetanus. The haptophore group has already had time to fix on the receptors before the antitoxin could neutralise it, and in that way the toxophore group, as soon as the temperature permits, is allowed to get into action.

If only small doses of toxin are introduced into an organism, the haptophores will unite with some of the receptors of the cells.

According to the law of Weigert, all destruction in the organic world is followed by a hyper-production. In this case also the lost receptors are replaced by a larger number of new receptors thrown out by the functional nucleus (Leistungskern). If the doses of toxin are now gradually increased, the number of receptors becomes so great that they are torn off from the cells and circulate as so-called "free receptors" in the blood-stream of the animal. These free receptors retain their power of uniting with the haptophore groups of the toxin, and by that way counteract the toxins. *Therefore the antitoxic sera are nothing else but sera which contain a large quantity of free floating receptors,* to which the haptophores of the toxins present in the patient are fixed, in this way preventing these haptophores from getting attached to receptors, which are still adherent to their cells, thus depriving them of their deleterious effect.

A similar theory applies to the bacterial immunity. The anti-bodies of the blood are not simple in their structure, but consist mainly of two parts of the amboceptor, or, as Metschnikoff terms it, "fixateur" or "substance sensibilitatrice," or, as Sir Almroth Wright terms it, "incitor element." This is a thermo-stable or resistant substance which only appears in the blood after it has been in contact with the organism or organic substance, for which it has its specific action. Any such substance, whether bacterial or otherwise, which is capable of producing anti-bodies in the blood we call "antigen." In an immunised system the antigen combines with the amboceptor, but this alone would not be able to produce immunity. There is a second factor to it which is called the "complement," and only by the common action of comple-

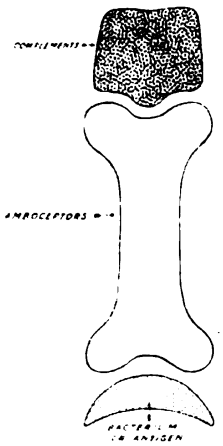


FIG. 3.

ment and amboceptor, the immunity, respectively the annihilation of the antigen, is produced. The complement is found to a certain extent also in animal bloods without any contact with an antigen, but it is a very sensitive structure, which is easily destroyed by heat, light, or even by being kept *in vitro* for some time.

In Fig. 3 the co-action of amboceptor and complement is represented. In this diagram it is shown how an amboceptor combines with the bacterium, or with the antigen, as the case may be, and is joined on the other side by its complement.

This theory applies, with slight alterations, to practically all anti-bodies. It will now at once be clear what is meant in the table by a "true immunity," which, as stated before, is due to an absence of anti-bodies. It simply means that in certain animals which have this so-called "true immunity," the functional nuclei of the cells have no appropriate receptors for those toxins for which they are immune. In consequence the haptophore

group of these toxins cannot get any hold on the cells, and accordingly the toxophore group cannot exert its fatal action. This is the reason why in these animals such toxins remain in the circulation practically unaltered for some considerable time without affecting the animal itself.

The immunity which is acquired by having survived the disease is also easily understood, as in the disease a large quantity of amboceptors is formed owing to the contact with the organisms, and these remain in the system for a longer or shorter period. Of course, if an overwhelming amount of organisms or toxins is suddenly introduced into the system the blood is not able to produce amboceptors or receptors, as the case may be, quickly enough, and in these cases the individual succumbs to the disease. If the disease lasts for some time, a race between the invading organisms and the production of amboceptors takes place, and then it depends whether the microbes succeed to multiply faster than the amboceptors are formed, in which case, of course, it gives a fatal end for the invaded system; or whether the blood produces amboceptors quickly enough to destroy the bacteria before they have time to overcrowd the system, with the result that the patient recovers.

In those cases in which opsonins or tropines come into action also the number of phagocytes and their vitality is of no little importance. The latter, as we know, can be greatly reduced by various causes, as constitutional disease, especially by chronic alcoholism and morphia mania, in which cases, of course, the production of opsonins is futile, as the bacteria might be well prepared for phagocytosis by the opsonins and yet not be taken up by the leucocytes owing to their own bad condition.

In other cases, again, the functional nuclei are able to throw out receptors, or the blood is able to produce amboceptors in a sufficient quantity to overcome one attack of the disease, but then exhaustion takes place, and it requires some time before they have sufficiently recovered to produce fresh anti-bodies, and during this time the individual is in a more or less defenceless condition and liable to any fresh infection of the same kind. This is one of the explanations of the fact that certain diseases leave the system not in a condition of immunity but of hyper-sensibility of a fresh attack (pneumonia, influenza, etc.).

It would not be within the limits of this paper to go into further details of the theory, which, although they might make one or the other point clearer, would complicate a good many others, and in this way might be confusing. The object was only to give a short and in no way complete exposition of a very extensive and complicated matter.

August 16th, 1909.

A CASE OF ABSCESS OF LIVER.*

By ALEXANDER DON, M.A., M.B., C.M., F.R.C.S.,
Surgeon to and Lecturer on Clinical Surgery in the Royal Infirmary, Dundee.

THIS disease is so rare in this part of the country, notwithstanding our close business relations with India, that I thought it worth while bringing it before you. It also happens that this very subject occupied a good space in last week's 'British Medical Journal,' and those of you who read through the rather long series of articles and the discussion thereon will not be surprised that this case, too, has given rise to some diversity of opinion. I saw the patient first in consultation with Dr. Clark on February 22nd, 1907, and from the history and signs we agreed that there was probably a liver abscess, and I proposed taking him into the infirmary for operation. He was averse to operation, but ultimately he came into my ward on February 24th of this year.

The history of his illness was as follows: On October 1st, 1907, he had to leave off work owing to feeling sick, weak, and ill for a whole week. He returned to work at the end of a fortnight, but while working he felt tired, and after seven days had to stop working a second time. This time he was off for three weeks, feeling sick as before, and pained in the pit of the stomach. Pain was steady and severe, and unaffected by food or posture. He also had an aching pain on the right side of the chest beginning at the lowest rib, and shooting up over the clavicle to the posterior triangle of the neck, stopping short just behind the right ear. This condition passed off, and he returned to work, and remained till three days after the New Year, during the whole of which period he felt well. Then a recurrence of his former affection again incapacitated him. After being off work for a month he started again, and continued till a few days ago. While at work he felt well. He was seized with a dull pain over the whole of the back, but worst at the small of the back. Next day the pain in the side of the chest returned. This pain is unaffected by deep inspiration, but is made more severe by coughing.

* Delivered before the Forfar Medical Association.

He thinks the pain is easier when he is walking about.

Previous illnesses.—Measles and whooping-cough as a child. Inflammation of lungs twelve years ago. Dysentery in South Africa for six months, four years ago. Gonorrhœa ten years ago. Other venereal trouble denied. No accidents.

Family history.—Father dead, age and cause unknown. Patient is an illegitimate son.

Habits.—Patient is a joiner, æt. 32 years, and works mostly in the shop, which is well ventilated, the windows being kept open. He stands or walks about most of the day. On an average he drinks four cups of tea *per diem*. He has always been a non-smoker. He drinks a little beer or whisky, and has occasionally exceeded.

Examination.—Nothing abnormal was noted on inspection of the chest or of the abdomen, which were well formed and of good contour. When asked to indicate the painful place, he marked out a triangular area, limited by a horizontal line through the right nipple, a vertical line through the right nipple and the right costal margin. On strong palpation over this area there was tenderness. On percussion the liver was found to extend in the mammary line from the fifth interspace to the costal margin, and in the mid-axillary line from the sixth rib. No enlargement of spleen.

Alimentary system.—No anomaly. Bowels are constipated, and have always been so.

Circulatory system. — On inspection nothing abnormal. On palpation a thrill over the præcordia, systolic in time. Apex-beat in fifth interspace $\frac{1}{2}$ in. internal to the nipple.

On percussion the right side of the heart reaches the right lateral sternal line; the upper border, the third interspace; the left border is within the mammary line.

On auscultation a systolic rough murmur is heard in all areas but the tricuspid, and is propagated along the vessels and to some extent down the sternum, but not into the axilla. Pulse 78, regular, small, slow rise, apex not sustained, sudden fall. Vessel walls not thickened.

Respiratory system.—Dulness, diminished breath-sounds, and friction over the lowest lobe of the right lung, below the angle of the scapula and in front. Elsewhere results of examination are normal, also friction over the pleura covering the liver.

February 26th.—Dr. M. Whyte found crepitation apparently superficial like dry pleurisy and he thought it might be tubercular, and he was transferred to his ward, when the following notes were added:

March 1st.—Patient complains of pain which shifts above over the right side. Pain is not so severe as it was.

Examination shows impairment of note in right side behind, below the angle of the scapula, and to some extent in the right axillary region. No dulness at apex.

Auscultation.—Breathing over right lower lobe and in right axilla (lower part) is accompanied by coarse creaking friction-rub. Breathing is vesicular all over the chest. No signs of phthisis: no accompaniments.

He was discharged on March 19th, and returned on April 21st. His condition then was: The pain was not very bad when he lay in bed, but was constantly present. It was worst when he took a long breath, or coughed. It was not associated with cough, however, and there was no spit. He was not troubled with breathlessness. He slept well, but for some time had not been taking his food so well as formerly. The bowels were regular.

Examination of chest.—Chest expansion appeared equal on both sides. Percussion detected dulness on the right side at the level of the fourth interspace in the nipple line, and passing round to the back at the level of the fifth rib in the mid-axillary line, and then in a curved line with the convexity upwards to the seventh dorsal spine. It was impossible to differentiate this dulness from liver dulness. Vocal fremitus was equal on both sides both in front and behind. (Note that the dulness is a space higher up now.)

Auscultation.—A few fine crepitations were heard on inspiration towards the upper margin of the area of dulness but were absent at the bases. In the mid-axillary line on deep breathing a soft friction-sound could occasionally be detected. The R.M. was perhaps a little harsher on the right lower lung than on the left, but there was no tubular or bronchial breathing. Vocal resonance was equal on both sides.

Circulatory system.—The pulse was 50 per minute at the wrist, very irregular, but full and sustained and of good tension. Beats appeared to be omitted at regular intervals.

Alimentary system.—Occasionally felt sick but never vomited. When sick he usually perspired and felt hot. He, however, did not have any shivering fits, but from his description these attacks did not seem to be unlike slight rigors.

April 22nd.—Still some pain at the ninth to tenth costal margin, and there was a feeling of resistance as if there was a small soft tumour about this region. Cammidge's pancreatic reaction was negative.

On April 23rd a good deal of impairment of resonance was noted over the right lung as compared with the left, but breath-sounds were practically similar. The liver dulness seemed increased upwards and there was still pain on pressure over the region of the gall-bladder. No fluid was obtained on aspiration through the chest wall.

April 24th.—Under chloroform and $\frac{1}{4}$ gr. morphia subcutaneously an incision was made between the ensiform cartilage and umbilicus. There was some slight hæmorrhage which was stopped by compression forceps, and the peritoneum was opened. The liver, transverse colon, and omentum showed in the wound. The gall-bladder was easily exposed a little to the right. The transverse colon was adherent to the gall-bladder from its middle. The adhesions were old and fibrous. The gall-bladder was normal. The wound was enlarged by a transverse incision through the right rectus a little above the umbilicus to allow of the ducts being more fully examined. The adhesions were freed between forceps and tied off, but as they were very close and numerous and as bleeding was free they were not separated in the depth. It was possible to pass the finger underneath the adhesions from the right side, but it did not enter the lesser cavity through the foramen of Winslow.

Palpation through the adhesions did not detect any calculus. The pancreas felt more nodular than normal and thicker, but unless any of these nodules was a calculus no cause for the attacks could be made out. The anterior convex surface of the liver was next examined; there were a few recent adhesions to the under surface of the diaphragm, and these were easily separated back to the falciform ligament on the right side, but nothing abnormal was detected in the liver either in appearance or in feel. The peritoneum was united by three catgut sutures over the bared surface of the gall-bladder to prevent reunion to the transverse colon, and the abdominal wound was closed by through-and-through silkworm-gut sutures. The skin was then united by a continuous button-hole suture of silk, and a gauze dressing applied. The patient was rather blue at the end of the operation and breathing was shallow, but the pulse was good. There was very little after-sickness.

April 25th.—Was complaining of a great deal of pain: "his back felt broken," he said. Did not sleep any last night. He had $\frac{1}{6}$ gr. of morphia, which relieved the pain. He did not complain of pain in the front of the abdomen at all. Temperature and pulse normal.

April 26th.—Had a very restless night. Even with $\frac{1}{6}$ gr. morphia he did not sleep, though the pain abated considerably. There was a good deal of tympanitis and the bandages were loosened. There was frequent vomiting of bile. A rectal tube was passed twice and left half an hour with some benefit, while a mixture of bismuth carbonate and acid hydrocyanic was given by the mouth. Peptonised milk was also given. Temperature remained normal, but the pulse-rate went up to 112 late at night.

April 27th.—A good deal better. Had an enema with pea-soupy stool. Some hiccough, but has abated since morning as has also the vomiting. He had $\frac{1}{6}$ gr. of morphia last night, about 8.30 p.m., and $\frac{1}{6}$ at 1 a.m. but did not sleep till after four this morning. Pulse was then 84 and temperature normal. Not so much distension.

He quickly improved, and went home a month later apparently quite well, and he had no further trouble till September. I saw him again with Dr. Clark on September 18th, and on September 19th, he was readmitted with diagnosis of abscess of liver. The following notes were taken by the house-surgeon.

Complaint.—Abdominal pain.

Duration.—Six weeks.

History.—He has now a sharp pain most marked about $2\frac{1}{2}$ inches outside the umbilicus on the right side, which seems to shoot upwards towards the right axilla but never goes further than the nipple. There is also a duller, deeper pain behind which shoots right up towards the ear, where it stops. Pain is increased on movement, being especially

painful on bending. He has also occasional pain over the gall-bladder. He vomited three times before he came in, and put up about two mouthfuls each time of bile-stained material. Taking of food has no effect on pain. Suspicion of jaundice at one time. Slight attack; no definite history.

Abdominal examination.—Stomach extends to a little above the umbilicus. Spleen does not appear to be enlarged. Tender spot with increased resistance slightly to right in infra-sternal notch. Liver, from fourth rib to half an inch below costal margin, palpable subcostally. Slight dulness over the gall-bladder, which point is also tender. Note liver is now lower, and dulness higher.

September 23rd.—A radiogram of the thorax shows a shadow extending above the liver to the third rib in the mid-clavicular line in front of the chest on the right side.

On September 24th he was examined by the Röntgen rays again with the screen, both abdominally and through the chest. Nothing could be made out in the abdomen, and a plate was taken with the liver lifted well forward by a pillow under his back. On screen examination of the chest it was noted that the right side of the liver did not show any movement with respiration. The dome of the liver was a dark shadow raised up to the second interspace in front and to the angle of the scapula behind. On turning the patient round it was noted that the shadow followed the anterior, external and posterior chest wall, and was joined on to the cardiac dulness internally.

September 26th.—There is a leucocytosis of 29,080. The cells are almost entirely polymorphonuclear, with a few lymphocytes. The hæmoglobin is 90 per cent.; erythrocytes 3,683,000. The case had been diagnosed as probably an abscess of the liver, but Professor Marshall, who saw him, thought it was merely thickened pleura, but considered exploration through the chest quite justifiable.

September 28th.—Under chloroform an incision was made through the sixth interspace in the axillary line. The pleura was entered and was found to be adherent over the dome of the diaphragm, but not firmly, and the pleural cavity was easily explored. The aspirating trocar and cannula was next entered through the diaphragmatic pleura and thick pus escaped very slowly. The pleural cavity was walled off with gauze and the trocar opening enlarged by the knife superficially, and then after Hilton's method by a pair of catch forceps. A drainage-tube was inserted. A good deal of thick, purulent matter came away. The rest of the wound was packed and dressed with gauze. Some of the pus was kept for examination by the house-surgeon, and was found to contain amœboid forms.

September 29th.—Had a fairly good night and there had been a good deal of discharge. He had $\frac{1}{6}$ gr. of morphia to ease the pain, which was pretty bad at one time. The dressing was removed. The discharge had come quite through the whole of the dressings. The discharge was very much bile-stained. A fresh dressing was put on, but the tube was not removed nor was the plugging round the opening taken out.

September 30th.—The discharge from the wound is a sticky, mucous, slightly blood-stained, thick discharge. There is considerable quantity, which soaks quite through the dressings each day—in fact the whole thing looks exactly like a profuse discharge from a cholecystostomy. The gauze packing was removed to-day round the tube, and a similar dressing applied.

October 1st.—Dressed again to-day. Still a considerable amount of discharge. When he turned round to-day there was a good deal of serous discharge came away after the thick mucous material. The bile-staining is not quite so marked as it was a day or two ago, but the discharge is more of a chocolate colour with a peculiar odour. It is less tenacious, more lumpy, as if it contained broken-down liver. No yellow pus.

October 11th.—Daily dressing, still discharging. Fresh culture taken. Discharge less. The tube was omitted on October 8th.

October 12th.—Marked rise of temperature. Fresh tube inserted. Patient has some headache.

October 14th.—Report on pus by Professor Sutherland: "No amœbæ, liver-cells, pus-cells, *Staphylococcus albus*." Patient is much better.

October 18th.—Patient is much better. He has been dressed daily since last rise of temperature. To-day a fresh tube was inserted. There is a good deal of chocolate-coloured discharge. His general health is fairly good, but he is anæmic. An iron tonic was prescribed.

October 20th.—There is very little change to record. The temperature occasionally rises to 100° F. and the pulse remains still about 100.

The discharge is still free, but is slightly more purulent and less of chocolate colour. A culture was taken to-day at the dressing.

October 27th.—Patient is feeling much better. Very little discharge compared with what it was previously, and thinner and less like chocolate. Eating and sleeping well. Pulse-rate coming down (80).

October 30th.—Culture shows no new growth since last time.

October 31st.—Leucocyte count taken. Leucocytosis 9685; polymorphs 71 per cent.; eosinophiles 3·25; lymphocytes 22·5; transitional 3·25 per cent.

November 10th.—There has been no discharge now for nearly a week, and he left the hospital well.

January 16th, 1909.—He has been at work for the past two months and has been feeling fairly well. There has been some slight swelling in his right foot at nights. Last night he complained of feeling cold when he came home from work and went to bed early. This morning, on getting up, he vomited a large quantity of blood and matter (?), and died in a few minutes. No post-mortem was allowed. The cause of death is therefore very obscure, as the matter said to have been vomited may not have been pus, and the blood may have come from either stomach or lungs, as no doctor was present at his death and the vomit was not examined.

This case shows remarkably well the chief points brought out by Sir Havelock Charles in his paper (1). We had all the diseases he enumerates for differential diagnosis, and most of these were thought of owing to the man having been abroad, viz. malaria, hepatitis, bowel troubles, cholangitis, pleural effusion, tuberculosis, gummata, biliary calculi, and new growths. At first he was treated for pleurisy, probably of tubercular origin, and with rest this subsided and he was discharged. The notes on his condition taken in the medical ward afford no indication of liver abscess except the friction-rub, and this was attributed to the pleurisy. Sir Havelock Charles notes the deceptiveness of auscultation, and in this case it was noted that on percussion the dulness was higher up than what the friction- and breath-sounds suggested. In other words, "the percussion area was not confirmed by auscultation." The notes say: "Breathing over the right lower lobe and in the right axilla (lower part) is accompanied by coarse, creaking friction-rub. Breathing is vesicular all over the chest. No signs of phthisis. No accompaniments." Rigors were entirely absent. There were more the digestive troubles, the sickness and the weakness, and the pain. The only suggestive pain was that shooting up to the neck, due probably to diaphragmatic pleurisy and referred along the phrenic nerve. Aspiration was negative, though probably the abscess may have been reached. The pus was very thick and would not have entered an ordinary small aspirating needle—in fact it would not flow through the biggest needle of the aspirator with the bottle well exhausted.

The examination of chest cases by Röntgenography should never be omitted where an installation is available. The amount of information obtainable has to be experienced to be believed, and here I would point out the uselessness of a cursory examination without the examiner having been for some time in the dark-room before he makes his examination. In this instance the shape of the dome absolutely excluded pleural effusion. The absence of movement showed great tension and fixation not seen in simple enlargement of the liver, and the pushing over of the heart suggested great pressure.

Sir Havelock Charles sums up as follows: "The variety in the symptoms of hepatic abscess is very great, therefore mistakes in diagnosis are common. The disease may pursue a latent course till the abscess ruptures into an adjacent organ, and the finding of the chocolate-coloured pus in the sputum or stool may be the first sign explanatory of the real trouble. Again, the abscess may be found only at death, showing it is often confused with other affections, and *vice-versâ*. Frequently, indeed, the symptoms but suggest, rather than point to, hepatic abscess."

He advocates in his operation excision of three or four inches of rib. I am averse to resection of ribs if it can be avoided. For a recent empyema when expansion of lung is probable, and liver abscess when expansion of lung to meet the rising liver is certain, there seems little need for resection. The cut rib may become infected, and sequestra have often to be removed, and it is seldom that adequate drainage cannot be obtained through the wide intercostal spaces in front. The mortality of the operation is also so high—40 per cent. to 60

per cent. in different parts of India, and this is often due to sepsis—that the less we open up fresh fields for organismal culture the more likely are the wounds to be kept clean. The appearance and smell of the pus are quite characteristic, and I regret that I could not have shown my patient to you a fortnight ago. It is like chewed chocolate, and the smell is mawkish and stronger than after a cholecystostomy. The presence of the amœbæ is vouched for by my house-surgeon, and it is quite likely that it may have been seen. Later cultures are not so reliable. Whether washing out the cavity with quinine would have helped I cannot tell, but there seems no reason to suppose it would. We managed to keep the cavity free from new organisms, and that cannot easily be done if irrigation or any elaborate form of treatment has to be carried on daily in a general surgical ward. Major Rogers (2) found that though in 80 per cent. of the cases the pus was sterile at the operation, only 25 per cent. remained sterile after three days, and 98 per cent. of those who died had very septic discharges. He has introduced a flexible drain for washing out and draining the cavity.

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August 16th, 1909.

GASTRIC DILATATION ASSOCIATED WITH EXTREME CYANOSIS.*

By GEORGE TEMPLETON, M.B., F.R.C.S.Eng.,

AND REMARKS THEREON BY

DR. LEONARD GUTHRIE.

MR. PRESIDENT AND GENTLEMEN,—The case which forms the subject of this communication presents features of a somewhat unusual character rendering an accurate diagnosis difficult. I have therefore thought it well that I should bring it to the notice of this Society.

* Delivered before the Medical Society of London.

It will generally be allowed that a dilated stomach at times offers considerable mechanical embarrassment to the heart's action, and in not a few instances palpitation and dyspnœa are observed. Cyanosis is not common except in cases of organic disease of the heart or respiratory obstruction. When, therefore, in the total absence of evidence of cardiac disease or respiratory obstruction intense cyanosis rapidly supervenes, and gastric phenomena appear and simulate rupture of an ulcer, I cannot but think that the points of such a case do not fall in line with the occurrence or description of which I have previously encountered.

A lady, æt. 28 years, belonging to a healthy family and personally of a robust constitution, had, three weeks previous to this illness, lost a near relative to whom she was much devoted and whom she had nursed practically unassisted through an illness of several months' duration. She always enjoyed her food, had only occasionally slight indigestion, and at intervals took a mild aperient.

Two days before the onset of the attack she had performed a tedious railway journey, and partook of luncheon on the train which she did not perfectly relish.

On her arrival in London her friends noticed that she was not in her usual good health and spirits. The following day she was listless and disinclined to eat or go out. She had some general abdominal discomfort but no sickness. Menstruation had occurred the previous week, and though subject to dysmenorrhœa the general abdominal discomfort referred to was of an entirely different character, affecting principally the epigastric region.

After a restless night she got up feeling still less inclined to go about. She spent the earlier part of the day on a couch and had a light milk pudding for luncheon. About four o'clock in the afternoon while receiving friends her appearance was observed to change suddenly, much to the alarm of those around.

Her naturally fresh complexion changed to a dusky blue, the lips became prune-juice coloured, and the extremities cold. Consciousness was retained perfectly and there was no rigidity or twitching. She complained of sharp abdominal pain in the region of the umbilicus, and vomited material which was not preserved but was said to contain nothing suggestive of blood.

The cyanosis increased till the face was almost

black, the lids becoming so puffy that her eyes were obscured, the lips were turgid, and the nose assumed a flat, negro-like appearance. There was no difficulty of breathing, but as time progressed she complained of severe pain across the upper part of the abdomen. She was removed to bed and a doctor summoned. Strychnine and ether were administered hypodermically, and hot applications were placed on the abdomen; the pulse was then of good quality and tension at 86; the bowels had acted in the morning. On arrival two hours after the commencement of the attack her condition had somewhat improved, the face was still deeply cyanosed and the eyes closed by œdema of the lids. The finger-nails were dusky, pulse 90. The knees were flexed, and severe pain was referred to the epigastric and right hypochondriac regions, which were considerably distended. Respirations were of a rapid, catchy description with diminution in diaphragmatic movement. A tympanitic note could be elicited over the area of distension; the liver dulness was reduced to two inches below the right nipple from this point. Tympanitis extended to a line two inches below the umbilicus. There was no stomach splash and flank dulness could not be detected. There was rigidity and some tenderness in the upper part of the abdomen; the pulse-rate was steadily increasing with a temperature of 97·8° F. A careful examination of the heart was made and neither dilatation nor bruit could be detected.

My general impression was that rupture of a gastric or duodenal ulcer had taken place, but in view of the extreme dilatation of the stomach and pronounced and persistent cyanosis in the absence of any apparently serious derangement of the heart I asked Dr. Leonard Guthrie to see the patient with me.

After consultation we considered it wise to open the abdomen for purposes of diagnosis, and if need be, treatment. This was done at 8 p.m., four hours after the onset of the illness.

Ether and chloroform were administered, and immediately the abdomen was opened by a median epigastric incision, which bled profusely, the tense anterior wall of the stomach presented, and coursing over its surface numerous engorged vessels were observed. Gas and free fluid were entirely absent from the peritoneal sac, and after withdrawing the stomach and systematically examining it from fundus to pylorus, no solution of continuity could be detected, nor was any localised thickening encountered suggestive of ulceration.

The duodenum was next investigated, with the same result—no perforation or ulcer. The stomach was not opened, but while outside the body the extreme congestion of its walls became considerably less, and the muscular tissue, in virtue of the oxygenation of the blood and the alteration in tension, appeared to improve in time, and the stomach became rapidly reduced in size and could without difficulty be returned within the abdomen.

The wound was completely closed in layers. The patient had by this time lost much of her cyanosis and the pulse had fallen to 80 per minute. Five minims of liquor strychninæ were injected subcutaneously and a pint of saline solution slowly introduced into the rectum.

The patient rapidly recovered from the anæsthesia and was not sick. Oxygen was administered at frequent intervals and had a decided effect in reducing the remaining cyanosis.

The œdema of the eyelids passed off the following day, but the tip of the nose and the finger-nails retained their blue tint for a week. Nitrite of sodium was given in three-grain doses three times a day. Rectal feeding was continued for two days and gradually feeding started by mouth. The distress which preceded operation was at once relieved, and steady progress was made to recovery.

Examination of the stomach by percussion at the end of a week demonstrated its return to normal dimensions. The bowels moved naturally the day following operation and no melæna was detected.

The patient has remained in good health since, now a matter of two and a half years.

The point which offers the greatest difficulty is to my mind the extreme cyanosis. There was no evidence of an epileptic seizure nor of the passage of food or other material into the larynx. Sickness commenced after the colour changed, and the epigastric discomfort increased to pain as in all probability the stomach became more and more dilated.

The great enlargement of this organ was very misleading, the extensive area of tympanitis inducing me to think that there was free gas in the peritoneal sac. The distension in the upper abdomen had not the appearance of that produced

by a much inflated stomach, and there was no splash to suggest that the case was one of simple dilatation. The sickness had, however, probably fairly thoroughly emptied the viscus.

The benefit attending the operation was very marked. I would attribute this partly to the copious hæmorrhage and partly to the oxygenation of the blood already alluded to.

I shall be interested to know if any of the Fellows have had a similar experience, and what explanation can be offered of such an alarming occurrence.

Dr. LEONARD GUTHRIE said it was not necessary, after Mr. Templeton's full and accurate description, for him (Dr. Guthrie) to say much about it. But he would offer one or two observations as his name had been mentioned in connection with it. When he saw the patient she was very considerably cyanosed : the lips and nails were purple, and the face bluish, and the œdema which had been referred to was disappearing. His first impression was that it was a case of acute dilatation of the heart. But the physical signs did not throw any light on or confirm that, neither were the symptoms such as would be associated with that. There was no increase in cardiac dulness, no venous pulsation, no bruit, and, in fact, no signs of dilatation. The pulse was regular and of good volume, somewhat raised in frequency, but practically normal. She was not dyspnœic, and turning over in bed did not cause her to be breathless. The voice was not altered and there was no difficulty in utterance. The abdomen was as Mr. Templeton described it. The question arose as to what the condition was and what was to be done for it. He thought Mr. Templeton would agree that had it not been for the cyanosis probably the patient would have been left alone. But as the cyanosis was so extreme and as the cause was obscure it was decided to operate, with the result which had been set out. He thought it would be agreed that the probable cause was some form of toxæmia. The first thing one thought of was the possibility that she had been taking a member of the coal-tar group, such as phenacetin. When that class of drug first came into use there were a number of cases, and some were still met with. He gathered that the patient had been considerably upset by family bereavement, therefore it was likely that she had headaches and for them took antipyrin or a similar drug. The next possible cause of the cyanosis was that it was a toxæmia which converted the oxy-hæmoglobin into met-hæmoglobin. Several cases had been recorded in Germany, usually associated with chronic intestinal complaints, such as diarrhœa. Sulph-hæmoglobin had been discovered, and in some others the spectroscope showed met-hæmoglobinæmia. It had been said that there was some microbic agent at work. In one very interesting case described by Gibson and Douglas there was a lady who was cyanotic for many months, and examination of the blood revealed the presence of a bacillus which resembled the colon bacillus. In time, after the treatment of the intestinal condition, the cyanosis disappeared. What was the connection between the dilatation of the stomach and the cyanosis? Was it that gas was generated in the stomach and absorbed into the blood, or was the stomach distended by gas, which escaped from the blood into the stomach? He did not know what occurred. And as the lady suffered considerably from malaise there was probably some form of intestinal toxæmia going on, and probably the dilatation of the stomach was secondary to that. The success of the operation was undoubted, but the explanation was not so easy. Was the benefit due to the loss of blood? Though, if such a case were met with again probably the same course would be followed, it occurred to him whether simple venesection would have been as beneficial. In any case Mr. Templeton was to be congratulated on the success of his operation.

Mr. TEMPLETON, in reply, said the question of the taking of coal-tar drugs was carefully gone into, and it was not found that she had taken anything except an occasional aperient when required. She had not had headaches. He believed the theory of toxæmia was the most likely explanation. It must be remembered that she travelled and ate a railway luncheon, which it was known sometimes contained ptomaines in a fairly virulent form. He had not an opportunity of examining the blood during the attack, but he now regretted he had not taken steps to have that carried out. From watching the case he was clearly of opinion that the dilatation very rapidly increased after the cyanosis had asserted itself; he therefore took it that there was an escape of gas into the stomach, possibly from the peculiar condition of the blood. The relief from the operation was probably due more to the hæmorrhage which occurred from the wound than from any other cause.

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A CLINICAL LECTURE

ON

OBSCURE FRACTURES.

Delivered at the Medical Graduates' College and Polyclinic.

By EDRED M. CORNER, M.A., M.B., M.C., F.R.C.S.,

Surgeon to the Children's Hospital, Great Ormond Street; Surgeon in Charge of Out-patients, St. Thomas's Hospital.

GENTLEMEN,—This afternoon I intend to bring before you some examples of what I have termed "obscure fracture." I chose that name because cases turned up undiagonised in my private and hospital practice. We have to appreciate that we are nowadays discovering fractures in cases where our forefathers in the profession would never have dreamed of their existence, so that, first of all, we must admit that there is a limit to our personal powers of diagnosis. Our forefathers in the profession had to diagnose cases by means of examination with their hands. We have now to learn the lesson that there are a certain number of fractures which we cannot diagnose by any examination with our hands. It is owing to this that they escape diagnosis, but they are becoming recognised and form an important division of injuries, which I have termed "obscure fractures."

I want to exclude one set of cases from these obscure fractures. I want to exclude absolutely those cases where the fracture is not diagnosed through a faulty examination or through carelessless; that is not meant. By "obscure fracture" I mean a case in which, after a full examination, the extent of the injury is still unknown. For the diagnosis of these fractures the X rays have become of the greatest use, and they have taught us of the existence of fractures of which we, like our forefathers, had no knowledge.

Before I show you some twenty-five lantern-

slides I want to tell you a little about them. The class of case in which these fractures are discovered are sprains. You get a person and he says he has sprained his elbow, or you get another one who has sprained his wrist, back, or ankle. Then those cases, instead of getting well in a short time, as a sprain should do, will not get well. So that the cases to which one would particularly attract your attention are cases of injury which do not get well quickly, and if these cases are examined by means of X rays and skiagraphs are taken, then often fractures will be discovered. This has an important bearing; the existence of these fractures should be known before giving prognosis and treatment. For instance, if a person has only sprained his wrist, he will get well in a short time, but if that person has broken some bones in the wrist, then his illness will be a great deal longer, and his recovery imperfect.

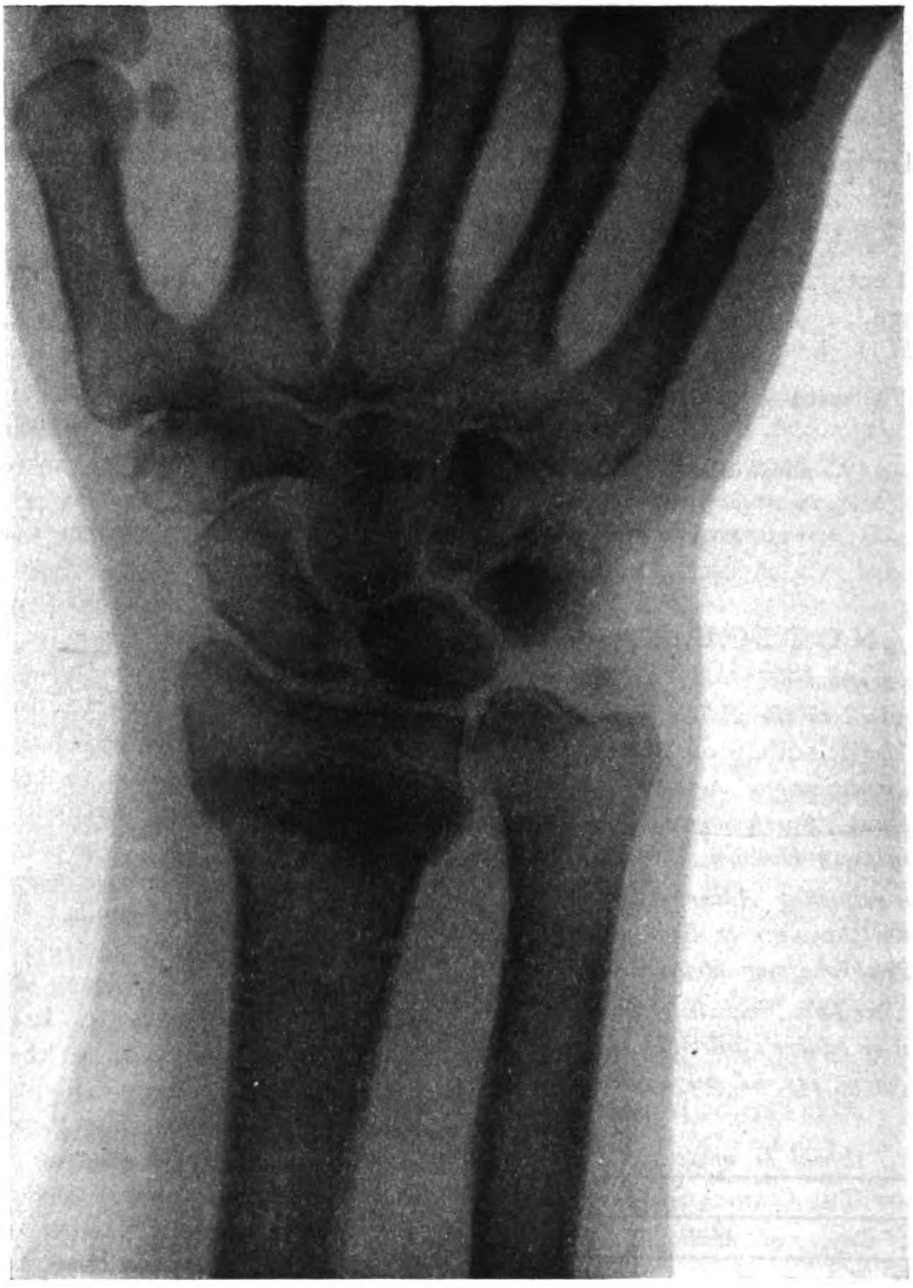

FIG. 1.—Impacted Colles' fracture.

There is another occasion where the knowledge

of these obscure fractures is of importance—injuries under the Workmen's Compensation Act. A number of cases are referred to us by employers or by insurance companies. A common history is that a workman sustains some injury which is certified as a bruised hand or foot. That workman does not get well. A month or two may elapse, and still the injured part is disabled and the man cannot work. The employer and the insurance company naturally object to paying, and regard the man as a malingerer. That is quite a typical kind of case in which, on X-ray examination, we find fractures which prove quite definitely that the man is not a malingerer, and that the employer and the insurance company will have to go on paying for some time.

There is another awkward point that crops up. When one of these obscure fractures is found we are asked by the insurance company or the employer, or perhaps by the judge or jury, "How long is this fracture going to disable the man; how long will it be before he gets well; will he ever get perfectly well?" Unfortunately we do not know a great deal about these fractures as yet. We do not know what the length of their convalescence will be, or the amount of future disablement which will result from them. Hence it is difficult and of practical importance for us to give a definite and authoritative statement to the insurance company, to the employer, or to the judge.

There is a last point to refer to. A doctor, for example, has a patient who says he has injured his foot. He examines the foot and says: "There are no bones broken; it will get well." Perhaps it gets well so slowly that the patient is dissatisfied and goes round to a chemist or somebody else who has an X-ray apparatus and a skiagraph is taken; and perhaps the man has had a fracture all the time. What is the patient to think of his doctor? These obscure fractures are not infrequently a source of malpraxis actions. In the hypothetical cases which I have mentioned the only fault of the doctor was that he did not have an X-ray taken himself; by his supineness he allowed his patient to have it done and to discover the "obscure fracture."

I have told you the class of case in which these fractures are found; cases of injury with sprains which do not get well. For us fortunately these obscure fractures group themselves into parts of the body, and it is to illustrate a few of the obscure fractures found in those different situations that I have brought together a collection of lantern-slides. One does not pretend that the selection is complete, but simply that the slides represent typical obscure injuries in the particular region. All the slides shown you have been taken from cases in which the injury was not diagnosed, and therefore come under my definition of "obscure fractures."

This is a slide of a well-known fracture at the lower end of the radius—Colles' fracture—which we have all seen and treated (Fig. 1). It was the case of a woman, æt. between 40 or 50 years, who fell down, and according to the diagnosis made by her doctor, "sprained her wrist." That sprained wrist did not get well; it was weak, painful, she had no strength in it, and could not use her arm much. At the same time her hand was deflected a great deal towards the radial side, so that she had to try and do her work very awkwardly. She came up to the hospital after three or four months, dissatisfied with her doctor. By then the swelling around the wrist, which would prevent her doctor making a correct diagnosis, had largely gone. There was sufficient evidence to suggest to me the advisability of having a skiagraph taken, which revealed an impacted Colles' fracture. There has been a great deal of discussion, and there is a great diversity of opinion as to whether Colles' fractures are often impacted or unimpacted. To answer that question I will divide cases of Colles' fracture in two groups—the diagnosed Colles' fracture and the undiagnosed Colles' fracture. The diagnosed Colles' fracture is sometimes impacted and more often not impacted. The undiagnosed Colles' fracture is always impacted. That is the answer at present to the question as to how often Colles' fractures are impacted.

The next slide illustrates a similar case to the first. It is from the skiagraph of the hand of a woman who fell and "sprained her wrist." The condition was undiagnosed. The case was a somewhat important one, that of a maid in the employ of a wealthy fruit merchant. I think she fell down the kitchen stairs and hurt her wrist. A doctor was called and said it was a sprained wrist and there was no fracture. A month or more passed and the wrist had not recovered as it ought

to have done. Her employer decided that this maid was taking advantage of the Compensation Act and discharged her. When she was discharged from his employ she had very little means of support and came to the hospital; and it was not till then—two or three months after the injury—that a true diagnosis was made. Before she came up to the hospital she had consulted a solicitor with a view of bringing an action. At the hospital I discovered the true state of affairs and communicated with her doctor, whose manners did not allow him to acknowledge the courtesy. But that particular case must have led to a great deal of trouble between the doctor, the employer and the employee.

To show you how frequent these impacted Colles' fractures are, I may tell you that in private practice I have seen two Colles' fractures within one week, from one family, from one house, and from one doctor's practice. Both were impacted Colles' fractures and both were undiagnosed. So that the first of these obscure fractures, from the practical point of view, is the impacted Colles' fracture. Whilst speaking of that subject I should like to point out to you a quite unrecognised injury. A young person has the epiphysis at the lower end of the radius, separated from the shaft by a layer of soft growing cartilage—the epiphysial line. If he falls on his hand he may drive the shaft of the bone through the cartilage into the epiphysis. That injury, which I would call an *impacted epiphysis*, shows itself more frequently as a somewhat thin, irregular, and indistinct epiphysial line. In some skiagraphs it looks as though there was going to be premature union between the epiphysis and the shaft. These cases are amongst the obscure fractures, and one would call them purely cases of impacted epiphysis. They occur in young people, and correspond with an impacted Colles' fracture which occurs in older patients. If there is a large swelling, the diagnosis of an impacted Colles' fracture is beyond the capability of manual diagnosis. To recognise an impacted epiphysis is more difficult. When there is a lot of swelling it is best to examine the injured part on the fluorescent screen, or, at least, make a point of suggesting it before the patient is allowed to have a skiagraph done and discover a fracture on his own account.

This is a skiagraph of the wrist-joint of a young patient. You can see still the epiphyses imperfectly united with the shaft bone. You can also see that there is still a good deal of cartilage round about the metacarpals and some of the carpal bones themselves. That was taken from a boy who, in common parlance, had "sprained his wrist." There was a lot of swelling at the time, making it quite impossible to ascertain how much damage had been done. The only thing one was sure of was that there was a considerable injury. If you look at this slide you will see, with the skiagraph taken in that position, front view, that it really does not show any very obvious trace of injury. It is when you look at this other slide that the forearm bones are seen to project forward and the lower epiphysis of the radius to be displaced backwards. That boy's hand and wrist were so swollen that it was utterly impossible to diagnose his injury before the skiagraphs were taken. It is another example of obscure fractures about the wrist.

This is a slide made from the skiagraph of a hand. There is an impacted fracture of the lower end of the shaft of the radius a little higher up than a Colles' fracture ought to be. That is another example of injury to the wrist whose explanation was only found when the skiagraph was taken.

This is another example of an obscure fracture about the wrist. It is from a person with a "sprained wrist." You will notice a very unusual fracture, which is shown simply because it was an obscure fracture in a wrist, in which a fragment was broken off the lower end of the ulna. In that swollen wrist there was no human means of diagnosing the condition until a skiagraph was taken.

This is a skiagraph of the elbow of a young subject. The arrow points to the elbow-joint to show that there was a fracture of the olecranon on the same level as the joint itself. So that, in a skiagraph taken in this anterior view, the X-rays go straight through both the elbow-joint and the fracture. After the obscure fracture in the neighbourhood of the wrist, the next most frequent in the arm is rather surprising, namely, fracture of the olecranon. Students are generally brought up to the belief that fractures of the olecranon are fairly easily diagnosed. As a matter of fact, it is quite wrong. I have found a large number of such fractures in bruised elbows, of which this slide

shows an example. There you will notice a fragment broken off the olecranon. At the same time there has been a fracture of the lower end of the humerus. With those two injuries the man came up to the hospital on a mere off-chance, having bruised his elbow some weeks before and taken no notice of it. In that bruised elbow were found these fractures.

This is another example of obscure fracture which was found in a man who had fallen and bruised his elbow. The reason why he did not get well quickly is obvious. He has a fracture through his olecranon on a level with the joint with very little displacement of the fracture. He was a postman, engaged as a temporary man, and had injured himself. The Post Office authorities thought that the man was a malingerer, and did not want to go on paying. It was not until the fracture had been found that it was possible to say that the man was not a malingerer, and that his convalescence would still go on for some little time.

This patient had been sent to St. Thomas's Hospital. He had fallen on his elbow and bruised it some weeks before, but his elbow did not get well. The explanation for his elbow not getting well is seen in that fractured olecranon.

This is a curious slide. You see the humerus, the broken-off olecranon, the radius and the ulna. You will notice on the surface of the skin some irregularities—a fluffy kind of stuff. That is zinc ointment, which had been put on the elbow by the patient. He came to my out-patients with an open wound over his elbow, from which was discharged pus and synovial fluid. A few weeks before, he had fallen, hurting his elbow, but had not regarded it as serious. His elbow had been fairly painful, but not sufficiently so to make him give up his work. A few days before he came up to the hospital he had been making a more violent exertion than usual, when the skin over his elbow had broken—that was what made him come to the hospital. The break in the skin communicated with and was followed by suppuration in his joint, the result of an undiagnosed fracture of the olecranon.

This is a curious case concerning which I should like to have had more time to speak to you. It is a skiagraph of an elbow-joint. You will notice a crack in the olceranon. It is a question what that crack is. The X-ray expert who took the skiagraph says that there was no sign of anything abnormal. But there might well be something abnormal because the boy had hurt that elbow twice. The first injury had been some months beforehand and his elbow had been bad for a month. A boy does not have a bad elbow for a month without a very good reason. Then he hurt his elbow again and the part remained painful; that is why I saw him. If that crack represents, as the X-ray people say, the epiphysial line, where are the epiphysial lines in the humerus and the radius? As the radial and humeral epiphyses have united, I think that the crack in the olecranon represents *a "tearing-off" of a freshly united epiphysis from the shaft* (Fig. 2).

This is another elbow. You will notice a kind of double epiphysis to the olecranon, which certainly is an epiphysis because the epiphysis at the head of his radius is present. It possibly represents a *fractured epiphysis.* I have been able to show you several slides in which a fracture of the olecranon was found in the elbows of people who thought they had only bruised them.

This is a skiagraph of an elbow showing the ulna, the radius, and the humerus with a fracture. Injuries to the elbow are a very important class of case, particularly in children who injure the lower end of the humerus. It is a good rule always to suspect the presence of such a fracture after an injury to the elbow in children till you find it to be otherwise. In adults with injured elbows, the fracture when present occurs usually in the olecranon.

This was a very interesting case of a boy, æt. 5 or 6 years, who was running out of his nursery and fell over one or two stairs. The accident was very slight, and he did not cry as if he was hurt. But what happened was that the boy could not be induced to use the arm after the accident. The mother could not find anything wrong with the arm. She sent for her doctor, and he could not find anything wrong with it. In spite of treatment, still the boy would not use his arm and the doctor began to think that there might be some injury to his brachial plexus of a very serious nature. When I examined him I could find nothing very definite, except a tender point at the upper part of his humerus. Having found that, I suggested that a skiagraph should be taken, and on the

skiagraph at the tender place was found a dark line. That dark line represents a very rare injury according to our present knowledge. It is a greenstick fracture of the neck of the humerus. If we skiagraphed a number of injured shoulders in children, possibly we should not find it to be so rare an injury as it is now thought to be (Fig. 3).

This is not a good skiagraph. It is the skiagraph of a hip, and the X rays have had to go through a lot of tissue. The consequence is that it is very hard to get clear skiagraphs from which to make lantern-slides. But I had this done, although it is not a very good one, that I might be able to show you it. It is taken from a boy who helped a carter. He was riding on the tail-flap of a cart, when the man who was driving the cart shouted out to the boy to jump off and pick up something. He jumped off hurriedly and injured his hip. The man stopped the cart and the boy was only able to get on again with difficulty. That boy never came up to the hospital or sought any advice for upwards of four months. When he came to the hospital we found pain in the hip, limitation of movement, wasting of the thigh and buttock, etc.—in fact, the picture of early tuberculous disease of the hip. A skiagraph was taken, with this result: The neck of his femur is broken and displaced upwards. You can see that the line of the acetabulum, instead of being opposite the neck of the femur, is lower. What happened was that the boy, in jumping off the tail-flap of the cart, had a partial separation of the upper epiphysis of the femur. That is what accounted for his symptoms. I have had an opportunity of seeing several of these cases of separation of the upper epiphysis of the femur. They usually appear very obscure fractures and are diagnosed as tuberculous hip or coxa vara.

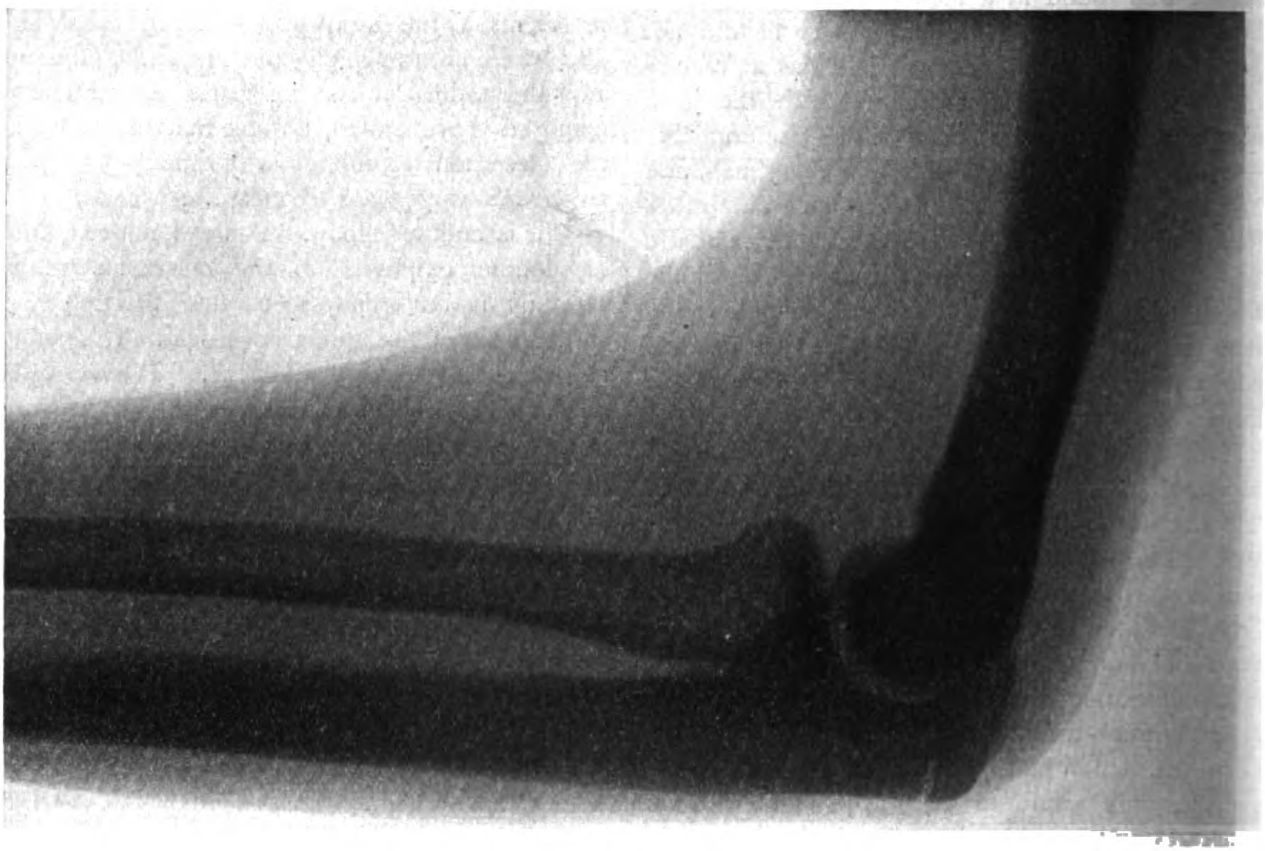

FIG. 2.—Tearing off of a freshly-united epiphysis.

This is an obscure fracture in the neighbourhood of the knee-joint. Obscure fractures are much

more common in the arm than in the leg, and much more common in the extremities of the

FIG. 3.—Greenstick fracture of the neck of the humerus.

limbs, namely, the hands and feet, than in the shoulder or hip. This man fell and hurt his knee. What was the matter with him was never known until a skiagraph was taken, when it was found that he had broken off the external tuberosity of his tibia. By no manual examination could we find the injury. You can see the line of the fracture and the broken-off fragment.

This is a skiagraph of a man who had an accident and came to the hospital a few days afterwards, saying that he had a pain in his leg. On manual examination of his leg we could find nothing. But we had a skiagraph taken, and even though this skiagraph was taken I doubt very much if any of you can see what is wrong. The picture shows that a "local chemist" who takes skiagraphs is not always a man who may be able to interpret them. If you look at this carefully you will see here a white line, and again at this place. It is a case of spiral fracture of the tibia. If one had not this skiagraph and was not able to demonstrate that fracture, the man would undoubtedly be condemned as a malingerer because we could not find out anything else wrong with him.

This is a case of injury to the ankle-joint. The slide is a very curious one, because it was taken when the leg was put up in plaster-of-Paris. The shadings are Bavarian flannel, and the dark line is the iron bar used to stiffen the flannel. It was a case of sprained ankle-joint. External examination could show nothing, but the skiagraph shows a fragment split off the lower end of the fibula. Before the X rays were introduced that man would, of course, have been said to have merely a sprained ankle, and if he had not got well quickly he would have been thought a malingerer.

This is a skiagraph of what is again a curious case, because he is a man who had an injury to his ankle some years before I saw him, and before the Employers' Liability Act had come into force at all. The result of the injury was that he could not go on with his work, and he lost both his employment and wages. There you see the tibia and the internal malleolus, and here the tibia and the external malleolus. Between the lower end of the fibula and the os calcis there is a large formation of new bone. That formation of new bone is presumptive of a former fracture. I have no doubt that this man who injured himself in pre-X-ray days had an "obscure fracture," and he lost his wage-earning capacity and job through hard luck. This is the foot of a man whose case came on in Court. He had hurt his foot in his employment, and he did not get well quickly, so that his employers (their insurance company) said the man was a malingerer. One had a skiagraph taken, and you see that prominence—it is a flake split off the outer surface of his os calcis. When that fact was pointed out the man was given time to convalesce, and finally got quite well. This case illustrates an injury which may well have been similar to that sustained by the man in pre-X-ray days, as narrated in the preceding case.

This is the foot of a man whose case went into a law court. He fell from a joist on which he was standing and hurt his foot. No fracture was discovered by manual examination. The man did not get well, but he was a good workmen, and therefore his employers had patience with the case. It was not till the skiagraph was taken that the true explanation was found. In the scaphoid bone there is a crack going right through antero-posteriorly. He had fracture of his scaphoid! That is an injury which we practically never heard of till X rays came in. Now that X rays have come in, we shall hear a great deal more about fracture of the scaphoid.

These last four slides are broken spines. When we learnt our surgery we learnt very impressively that a broken spine meant either death or paralysis for the rest of life. A great change is sweeping over that. Even in my own experience I have come across about ten or a dozen cases of broken cervical spine which recovered without any paralysis or anæsthesia whatsoever.* This slide represents a typical case of the kind. It shows the lower jaw, the skull, the atlas, and the axis, and the third to the seventh cervical vertebræ. We never knew of the existence of this fracture of the cervical spine till X rays came in. You will notice that the atlas bulges forward with the axis, and that case is probably—because one cannot tell the exact anatomy of the fracture—a fracture of the body of the axis vertebra with the odontoid process (Fig. 4). It comes under fractures of the odontoid process.† That man's history is very interesting. He had an injury at least four months before I saw him, and it was undiagnosed. The history obtained from him was that he fell on his head and hurt his neck; the neck was sprained and would not get well. It was that history that made me have a skiagraph taken to see what the injury was.

This is another fracture of the cervical spine. There you can see the jaw with some teeth, the skull, the atlas, the axis, and the third to the fifth

* *E.g.* 'Clin. Soc. Trans.,' 1905, vol. xxxix, pp. 212-213

† 'Med.-Chir. Trans.,' vol. xl.

FIG. 4.—Fracture of axis.

cervical vertebræ. You will notice again that the atlas with the upper part of the axis vertebra is displaced forward. That was taken from a case of neck injury—a boy who was shown at the Clinical Society some time after his accident. What was the precise nature of his injury I cannot say. But I can tell you that a normal cervical spine, instead of bulging forward, should be straight. So that there evidently has been some injury; and the injury in these obscure fractures of the spine usually—not always—occurs in the upper two cervical vertebræ. In the upper two cervical vertebræ the canal for the spinal canal is the largest, and apparently will allow considerable displacement without injury to the spinal cord.

The last two cases that I have to show you are examples of fractured spines in the lumbar region Obscure fractures in the lumbar region are not apparently as frequent as they are in the cervical region. In the spine, obscure fractures are more frequent in the cervical than in the other regions. In this slide you see represented the ribs, the ilia, and the lumbar vertebræ, one to five. I think the fracture is in the first lumbar vertebra. The case is that of a man, who as a foreman was one day standing on a heap of merchandise in the docks directing his men and was hit in the lumbar region by the swinging chain of a steam crane. He was a very good workman. The professional part of his history is very interesting. He was taken from the docks into the Seamen's Hospital where they kept him ten days. Four months after the injury the man's back was still weak and painful, he was unable to return to his work, and his employers, in view of the opinion given from the Seamen's Hospital, thought that although a good worker he must be malingering. But a fracture of the first lumbar vertebra was found, his employer told and advised to give the man further time to recover. His convalescence took about a year, after which he returned to his employment and is now doing his work as a foreman labourer as well as he ever did before. If it had not been for the discovery of that obscure injury by means of X rays that man would undoubtedly have lost his work and been condemned as a malingerer, and the fact that he recovered some months later would have made the people doubly sure that he had been malingering earlier.

This is another lumbar spine. There are the ribs, the ilia, and the first to the fifth lumbar vertebræ. The fracture you can see. If you look at the thickness of the first lumbar vertebra and compare it with the second you will notice that the second lumbar vertebra is about half the thickness of the first. There has been a fracture through the body of it. That suspicion is borne out by the fact that the vertebræ are not in a straight line; but at the second lumbar vertebra, instead of continuing its straight line, the axis of the spine goes off to the left. The case was a very interesting one. It was that of a young man, æt. 17 or 18 years, a seaman. When in Sydney, Australia, he fell down the hold of a ship. He was taken into the Sydney Hospital and kept there for ten days. In this skiagraph you see the last dorsal, the first lumbar and the second lumbar vertebræ are the broken bones. After that time he left the hospital but was no better; he could not do anything and his back hurt him. He was brought back to England and I saw him four months after the injury, when this skiagraph was taken. It took that young fellow about a year to recover, and now he is doing his full work as an able seaman. These last two cases show you that the convalescence from these obscure fractures takes about a year, which is an important point to know in giving a prognosis to the employer or to the insurance company.

There were two other cases of fracture of the lumbar spine which I had intended to show you. They occurred in a gentleman and a lady who fell out of windows 20 to 25 feet high. One happened in Ireland, and the injury not being diagnosed there the patient was brought over in a boat from Ireland to Holyhead, thence by train to London and on to a nursing home. So that there was a long and rough journey. It was not until six weeks afterwards that it was found that she had a fracture of the lumbar spine.

August 23rd, 1909.

THALER announces that the antitryptic index is exceptionally high in cases of puerperal fever with an unfavourable outcome. He found the Fuld method of determining the trypsin simple, convenient and reliable, the increase in the antitryptic index proving a valuable aid for diagnosis of pregnancy and for the prognosis of puerperal affections.—*Journ. A. M. A.*, vol. lii, No. 5.

A CLINICAL LECTURE

ON

ANTE-PARTUM HÆMORRHAGE.

Delivered at the London Hospital

By H. RUSSELL ANDREWS, M.D., B.S., M.R.C.P.,
Assistant Obstetric Physician to the Hospital.

GENTLEMEN,—I want to make some remarks this afternoon on the treatment of ante-partum hæmorrhage. I have chosen this subject because, although we get a good many cases in the wards every year, students do not, as a rule, see much of the treatment, as they are emergency cases requiring immediate treatment and often admitted during the night. Ante-partum hæmorrhage may be one of the most serious complications that can be met with in midwifery, the patient's life depending on the promptness and efficacy of the treatment.

As regards a description of what is meant by the term, I need not say much beyond stating the fact that ante-partum hæmorrhage is hæmorrhage due to too early separation of the placenta during the last two or three months of pregnancy, and that there are two varieties, namely, accidental hæmorrhage and placenta prævia or unavoidable hæmorrhage. If the placenta is situated on the lower uterine segment, it is prævia, *i. e.* in the way of the passage of the fœtus, and has to become partially detached during the process of dilatation of the lower uterine segment and cervix. Theoretically, this dilatation does not occur until labour has begun, but it is found practically that bleeding in cases of placenta prævia usually occurs before full term. If the placental site does not occupy any part of the lower uterine segment, bleeding from too early separation of the placenta is called "accidental hæmorrhage"—accidental because not a necessary phenomenon of labour. We will consider the treatment of this variety of hæmorrhage first.

If the separation occurs before labour has begun, the hæmorrhage may be concealed, the blood being pent up in the uterus, there being no uterine contractions to force it out of the uterus. If, on the other hand, the uterus contracts and expresses the blood, the condition is one of evident accidental hæmorrhage.

The diagnosis between the two varieties of ante-partum hæmorrhage can only be made by ascertaining whether or no the placenta is situated on the lower uterine segment, and in some cases cannot be made with certainty until the first stage is well advanced. Both varieties are rare in primigravidæ, so it is usually possible in a case of ante-partum hæmorrhage to insert a finger-tip and to ascertain whether the placenta is to be felt in the neighbourhood of the internal os or not. If the placenta cannot be felt in this way an examination should be made through the vaginal fornices. If the presenting part can be felt equally well through all parts of the vaginal vault, it is improbable that the placenta is situated on the lower uterine segment.

As regards the treatment of accidental hæmorrhage, when there is no evidence that the placenta is prævia, the bleeding is only slight and the pregnancy is still some weeks off full term, the best treatment to adopt is that which is employed in cases of threatened miscarriage, viz. to temporise in the hope that the bleeding will cease and the pregnancy continue to term. Before deciding to temporise, make sure that there is no evidence of concealed hæmorrhage by noting that the uterus is soft and not tender or distended, that the patient's general condition is not altered, and that the pulse-rate is not much quickened. Temporising, which is done in the interests of the child, means keeping the patient absolutely at rest in bed, administration of sedatives, the best of which is morphia, followed up, if necessary, by bromides and tincture of hyoscyamus, and avoidance of douches or enemata which might induce or increase uterine contractions. It is not uncommon to see such treatment successful, the bleeding ceasing and pregnancy continuing to full term. The appearance of the placenta in such cases shows that part of it has been detached too soon, some portion of it being brown, shrunken and more solid than the rest, and having some old blood-clot adhering to it. If there is more severe bleeding than this or evidence of retention of a large amount of blood in the uterus, temporising is not to be thought of, even though the fœtus has not yet reached a stage at which it is likely to be able to carry out an extra-uterine existence.

It is rare for accidental hæmorrhage to be entirely concealed. In most cases there is at

least a trickle of blood or of serum escaping from the vagina. If the uterus is distended with blood there are well-marked signs and symptoms which should lead to a correct diagnosis of accidental hæmorrhage, even though little, if any, blood can be seen escaping externally. The uterus becomes tense, globular and tender to the touch, and the patient complains of great pain, which she may describe as "stretching" or "tearing" pain. Her pulse becomes rapid and feeble, her expression is what is generally described as "anxious," and it is obvious that she is gravely ill. In evident accidental hæmorrhage, abdominal examination may not reveal anything unusual about the condition of the uterus, but if the amount of blood lost is large she will be collapsed and blanched with frequent feeble pulse, fainting, etc.

What is to be done to stop the bleeding in severe accidental hæmorrhage, whether concealed or evident, when labour is not yet far advanced? The usual surgical method of arresting hæmorrhage is to apply pressure to the bleeding point if it is impossible to ligature or suture it. In hæmorrhage from placenta prævia we know where the bleeding point is, viz. in the lower uterine segment, and we can apply pressure to it either by version and pulling on the leg so that the half breech compresses the bleeding point, or by a Champetier de Ribes' bag, but in accidental hæmorrhage we do not know where the bleeding point is.

In all cases of severe ante-partum hæmorrhage the one thing that the accoucheur wishes for above all others is strong uterine contraction. If the uterus is contracting well labour will be advancing, and the fact that the uterus is contracting well is a proof that the woman is not suffering severely from shock or collapse; therefore any method of assisting delivery that is indicated by the conditions found on examination, *i. e.* presentation, size of os, membranes, whether ruptured or unruptured, etc., will probably be successful. If the os is nearly fully dilated completion of dilatation by the hand followed by version or delivery with forceps will probably put an end to the bleeding. But in bad cases of ante-partum hæmorrhage the accoucheur has usually not got good uterine contractions to help him. The patient is suffering from loss of blood, from shock or collapse, and her vitality is much diminished. The author of a French text-book on midwifery published in 1907 says: "It is necessary to aim at relieving the uterus of its contents as rapidly as possible. Any method of *accouchement forcé* may be too slow, and recourse to Cæsarean section may be necessary." In my opinion it would be sounder advice to say: "Any method of *accouchement forcé* would be too rapid." The patient's vitality is so much lowered that the superadded shock of rapid delivery would be likely to prove fatal. Forcible and rapid delivery is sometimes attended by alarming symptoms of collapse in healthy patients who have not lost blood, and it is a most unwise method of treatment in patients who are already suffering from shock.

Some years ago I saw two cases of accidental hæmorrhage, one chiefly concealed, the other evident, in which delivery was hastened as much as possible short of tearing or incising the patient's tissues, and the result in both cases was death of the mother very soon after the delivery of a dead child.

In the first case a multipara, æt. 35 years, began to bleed about an before her admission to hospital. The uterus was distended and tender, the pulse was rapid and feeble, and she looked very ill. The os was about the size of a shilling. For the next three hours two qualified men, a sister and a nurse gave up the whole of their time to the patient and worked hard. The membranes were ruptured, ergotin was injected and a tight abdominal binder was applied. The cervix was dilated by the fingers and then by the hand, and the child extracted by forceps two hours after her admission. One hour later the patient died in spite of injection of saline solution. She lost every little blood after admission, but her condition was such that she could not stand all the manipulation to which she was subjected.

In the other case the treatment adopted was practically the same except that delivery was affected by version instead of by forceps.

In such cases active treatment and hastening of delivery produce the most discouraging and humiliating results. You feel that the patient could not have done any worse if she had been left absolutely alone. You are dealing with an exhausted patient whose uterus is possibly paralysed by distension with blood. It *cannot* contract. You seem to be as it were between the devil and the deep sea. If you do not deliver her she dies of hæmorrhage; if you do deliver her she dies of

shock. Fortunately there is another method of treatment which usually stops the bleeding, while so far from endangering the patient's life by the addition of shock it allows her to recover from the effects of the loss of blood. We saw that, while in placenta prævia we are able to press on the bleeding point, in cases of accidental hæmorrhage we do not know what part of the uterine wall is bleeding. The thing to do is to press on every part of the uterine wall. This can be done by plugging the vagina and applying a binder and a T bandage. This is an old method of treatment, said to have been recommended as long ago as 1776 and revived in recent years especially by the Dublin School. Some obstetricians object to it, saying among other things that it may convert external into concealed hæmorrhage, that it may cause rupture of the uterus, that it is painful and that it is inefficacious because the plug soon becomes loose. Dr. Galabin advocated this method of treatment in the first edition of his text-book on midwifery published in 1886, but "as it was found by students that the suggestion of plugging the vagina was apt to lead to their rejection at examination, the recommendation was omitted in later editions." It is included again in the last edition. The evidence of those who have used this method frequently is entirely in its favour. It is not painless, neither is any method of assisting labour rapidly. It seldom, if ever, converts evident into concealed hæmorrhage. If it causes rupture of the uterus it is not the fault of the method but of the accoucheur who is carrying it out, and has not realised that it has been so successful as to cause violent contraction of the uterus. If the plug becomes loose and blood escapes by the side of it it is a proof that the method has not been carried out properly. Plugging is sometimes performed in a manner which is only an absurd travesty of the method. I have twice seen a patient sent up to the hospital with a note that the vagina had been plugged because of hæmorrhage. In one case the vagina contained two pocket handkerchiefs and in the other about enough cotton-wool to fill a tea-cup. To produce a satisfactory result the plugging must be performed systematically. Sterile gauze is probably the best substance to use, but, failing this, pledgets of cotton-wool, or linen rags will do if they have been rendered sterile. A surprisingly large quantity will be wanted. The bladder should be emptied before the plugs are inserted. The membranes should not be ruptured artificially, or there may be some danger of increased hæmorrhage before the plugging can have time to act. The perinæum should be retracted by a Sims' speculum or by the accoucheur's left hand while his right hand introduces the plugs. All the fornices should be filled as tightly as possible one after the other, then the whole vagina filled until the plugging material projects at the vulva. The application of a tight binder and a tight, strong T-bandage completes the plugging. The uterus is then compressed over every part of its surface and the pressure is too great for more blood to escape into its cavity. When the plug, binder and bandage are in position, and not till then, saline solution should be injected into the tissues. This must not be done until the bleeding has been stopped, otherwise it will only tend to increase the bleeding, and if the patient is receiving saline solution and losing blood she will not score by the exchange. The result of the plugging is, in most cases, to induce contractions of the uterus, but even if it did no more than stop the bleeding it would be well worth doing, because the patient would be tided over the next few hours, during which, with the help of warmth, saline solution, etc., she would recover from her collapse and be in a condition in which any necessary assistance to delivery could be given with impunity. If uterine contractions are induced the plug should of course be removed before it can possibly cause any obstruction to delivery. After removing the plug labour can, as a rule, be allowed to proceed naturally. The plug should not be allowed to remain *in situ* for more than twenty-four hours. When it is taken out it is usually found that the cervix has become dilated to a greater or less extent, when labour can be left to take its course without further interference, or may be assisted by forceps or version if indicated. Delivery is generally accomplished without much delay, but in some cases although the bleeding ceases the uterus does not contract strongly. A primigravida was admitted into Helene Raphael Ward a few weeks ago with some accidental hæmorrhage three weeks before full term, blanched and faint. There was no appreciable dilatation of the os. The vagina was plugged and the bleeding ceased.

The plug was left in less than twenty-four hours, and as the bleeding did not recur nothing further was done. The patient was delivered naturally on the fourth day.

As regards treatment of placenta prævia, the first point is that it is not safe to temporise, however slight the bleeding may be. Although the bleeding may, and often does cease temporarily, it is impossible to prophecy that it will not come on again at any time, and when it does come on again it may be so severe that slight delay in treatment may be fatal.

I will quote a case which occurred in this hospital several years ago. The patient was at full term, the breech was presenting, and she lost a large quantity of blood from a placenta prævia. The resident accoucheur was sent for, and, when he arrived, found that the bleeding had ceased. He sent the patient up to the hospital, postponing any treatment until she should arrive in the ward. Very little time was lost, but when the patient reached the ward she was bleeding again, and so severely that she died in a few hours. If a leg had been brought down or a Champetier de Ribes' bag inserted it is probable that the patient would have lost no more blood after she had been seen first, and her life would have been saved. I always warn resident accoucheurs not to send patients with placenta prævia into hospital from the district without first adopting some measures to prevent hæmorrhage. As we saw before it is possible, if labour is sufficiently far advanced for the cervix to admit two fingers, to arrest hæmorrhage from placenta prævia by bipolar version and bringing down a leg or by insertion of a Champetier's bag. The former may be looked on as the classical method of treating placenta prævia. If bleeding recurs after bipolar version the leg must be pulled on so as to press the half breech on to the placental site.

Plugging the vagina is sometimes advocated in placenta prævia. I think it is in most cases the best treatment for a midwife to carry out if she has to treat a case of placenta prævia in the absence of a doctor, but I think that direct compression of the placental site by the half breech or a bag is better treatment in the hands of a medical man.

Placenta prævia is rare in primigravidæ, so in the large majority of cases it is possible to force the finger through the os and then to dilate the cervix enough to admit two fingers. If one finger is admitted easily a Champetier's bag can be inserted. Two fingers must be inserted in the performance of bipolar version. The advantage of using a bag is that the chances of the infant surviving are rather greater. The membranes must of course be ruptured, or in the rare cases of central placenta prævia the placenta must be perforated, before the bag is inserted.

A few practical hints as to the use of the bag may not be out of place here. The bag will be unsatisfactory if it is not completely filled, is too small, or if it slips up above the head, and it will be a source of danger if it is too large. Bags of varying sizes are sold now by instrument-makers as "Champetier's" bags. The bag of proper size holds 17 ounces and measures 3½ inches across the top when distended. Measure the contents of the bag carefully and reject one which holds more or much less than 17 ounces, and measures more or less than 3½ inches across the top. If the bag is too small it will not dilate the cervix sufficiently to admit the head, and if it is too large there will be danger of rupture of the uterus. Boil the bag before using it. Instrument makers sometimes tell you that the bags will not stand boiling. This is incorrect. They will not stand boiling an indefinite number of times, but they will stand it three or four times as a rule. See that the tap is turned "on" when the bag is put into the steriliser or the bag will burst. Adopt some plan to enable you to tell when the bag is full, you cannot tell this by simply feeling the tension of the neck. If the bag is not completely filled, you will find that when it comes out there is not sufficient dilatation for immediate delivery, while if you try to pump more than the proper amount into the bag you will burst it if it is at all weak from age or frequent sterilisation. If the bag holds 17 ounces, start with 20 ounces in a graduated bowl and a full Higginson's syringe. When the Higginson's syringe is full and there are three ounces left in the bowl you know that the bag is full. This sounds almost childish, but if you start with only 17 ounces of fluid you will be almost certain to get some air pumped into the bag as well as water, and it will be likely to burst. I have often seen a bag come out only partially filled when the accoucheur thought he had filled it

completely. Fold up the bag carefully and hold it in the special forceps so that a small cone of the bag projects beyond the tips of the forceps. Lubricate it and insert it as gently as possible. If it does not go in easily because the head is in the way steer the bag forward under the head by directing the handles backwards. The bag must of course be above the placenta, not between it and its site. Having inserted it so far that the rings of the handles are close up to the vulva open the forceps, pump in two or three syringefuls, then undo the lock and remove the blades separately. If you withdraw the blades of the forceps before you have pumped any water into the bag you may withdraw the bag at the same time. Fill the bag completely and ascertain while it is being filled that it is well below the presenting part and resting on the lower uterine segment. If the head presents the bag may lie by the side of it so that as it fills it rises up a little with the edge of its upper end resting against the child's neck. If this happens the bag will not press on the placental site, and pulling on the bag will only cause the head to press on part of the placental site. Do not hang too great a weight on the tube attached to the bag or you will pull the tube off or burst the bag. A weight of 3 lb. is enough. Tie the weight to the tube above the tap, or you will possibly pull the tap out of the tube. As a rule, when the bag is in position and is pulled on no further bleeding will occur. Do not pull the bag out of the vagina without letting out some of the fluid or you may tear the perinæum. I have seen this done.

These are all practical points; I have seen all these accidents happen in actual practice. When the bag comes out you will be able to deliver immediately if necessary by version or forceps. Remember that the bag often displaces the presenting part. This is a matter of small moment, as internal version can be performed, the os being fully dilated. If, however, the head has been displaced, you may be able to steer it into the pelvis as the bag is being expressed.

A bag may cause rupture of the uterus, but I believe that if the child is viable, and the uterus consequently of fair size, and you rupture the membranes when you insert the bag, and do not choose a bag of larger dimensions than those which I mentioned, this accident will not occur. It is a good thing when rupturing the membranes to push up the presenting part a little so that it cannot act as a plug and prevent escape of liquor amnii.

The advantage of bipolar version is that the uterus is partly emptied, more retraction can take place, and consequently the wall of the lower uterine segment will not be so full of blood. However, the chances of the child in placenta prævia are not good at the best of times, and pulling on the half breech must diminish these chances.

Never deliver the head, whether fore-coming or after-coming, till the os is completely dilated, because in placenta prævia the wall of the lower uterine segment has a better blood-supply and is thicker than usual, and consequently will not dilate as readily as usual, and will tear more readily. In some continental clinics there is a rule that the after-coming head must never be delivered by pulling until it is past the external os. It is considered that the practically certain death of the child is less to be deplored than is the risk of a tear of the cervix and possibly of the lower uterine segment.

When pressure by the bag or by the half breech has stopped the bleeding injections of saline solution can be given to treat the collapse.

Lastly, let me emphasise the importance of asepsis and antiseptics in the treatment of antepartum hæmorrhage. After severe hæmorrhage the patient's resistance is lowered, and an infection which would be met by a normal resistance may have grave and even fatal results. With so much manipulation there must be an additional risk of sepsis. Do not let rapidity be gained at the expense of asepsis.

August 23rd, 1909.

The Sero-reaction to Syphilis in the Cadaver.—The findings were positive in twenty-eight and negative in seventy-two of cadavers examined, the details of the cases showing that the Wassermann test is a useful aid in pathological anatomical research. At the same time, diseases causing much debility, such as phthisis, sepsis and cancer, seem to induce a tendency to production of substances which give a positive reaction to the complement-fixation test.—*Journ. A.M.A.*, vol. liii, No. 5.

INTERNATIONAL CLINICS. Vols. III and IV, 18th Series. J. B. LIPPINCOTT Co., Philadelphia and London, 1908.

THE opening paper in the first volume is by Sir Dyce Duckworth (London), who touches briefly on the nature and treatment of sciatica. He describes many remedies which have proved useful in different cases, but does not add anything fresh to our knowledge of the subject. A number of the papers are of the same character—that is to say, they give a *resumé* of all that is known on the subject, which may equally well be gathered from the pages of a text-book. Other papers deal with fresh ideas and therapeutics, which are not in the text-books, and which may stimulate practitioners to new efforts. Dr. Paul Tissier (Paris), for instance, has found in fluoroform a "specific treatment" for whooping-cough. Many of us have seen the rise and fall of "cures" for this affection, but have still sufficient faith and hope to try another. Fluoroform has the formula $C_2H\ Fl_3$, and is obtained from the action of fluoride of silver on chloroform, bromoform or iodoform. An aqueous solution of the gas is used. Another type of article is illustrated in that of Mr. H. S. Clogg (London), who works on "pericolic inflammation." This is a clinical study of all the forms of inflammation occurring in and around the colon, including intestinal diverticula, septic ulceration, and tuberculous lesions. He has collected a large number of interesting cases, and in a full paper gives the practitioner an account of many affections, which, although rare, ought to be kept in mind in dealing with obscure cases of disease in the region of the colon. In a clinical lecture on "general paresis," Dr. Smith Ely Jelliffe (New York) gives a graphic account of some illustrative cases, pointing out the various aspects under which the disease presents itself. The difficulties met with in forming a diagnosis between functional and organic disease are discussed by Dr. G. L. Walton (Boston). He makes the interesting suggestion that some cases of temporary paralysis may be due to sudden localised œdema of the nervous centres controlling the part affected. In angio-neurotic subjects such attacks are now recognised as affecting other parts of the body.

In the second of these volumes Dr. J. A. Lichty (Pittsburg) discusses the medical and surgical treatment of gastric ulcer, based on an experience of 140 cases. This is a large number, but he does not state whether there was any difficulty in making an exact diagnosis. It is probable that many cases previously regarded as gastric ulcer are really examples of oozing of blood from the stomach—the gastrostaxis of Hale-White—and are unaccompanied by any definite ulceration. In statistical results it is important to exclude such cases from those of undoubted gastric ulcer. Dr. Lichty's method of treatment has been the usual one—rest and starvation—but he notes that in three cases frank hæmorrhage occurred from the stomach although feeding by the mouth had been stopped. He is rather doubtful about the advantages of Lenhartz's treatment of feeding up the patient, and his fears have rather prevented him giving it a full trial. The indications he gives for surgical treatment are as follows: (1) If perforation occurs; (2) if pyloric stenosis occurs, so that the nutrition of the patient is interfered with; and (3) in profound hæmorrhage (very rarely). Gastro-enterostomy is not the panacea it was thought to be five years ago, and he notes that in the clinic of the Mayos of Rochester the number of gastro-enterostomies is steadily declining. A fine paper on acute dilatation of the stomach by Dr. A. G. Nicholls (Montreal) is worthy of note. The condition during life is frequently overlooked but is easily recognised in the post-mortem room. He relates the case of a girl, æt. 13 years, who suffered from attacks of copious vomiting and finally died. At the necropsy the stomach was greatly distended, as was the duodenum as far as the point where it is crossed by the root of the mesentery and the superior mesenteric vessels. Beyond this point the duodenum and the rest of the intestines were collapsed and empty. This case, along with others of a similar character which he has seen, suggests that the acute dilatation may supervene on a chronic obstruction lower down in the alimentary tract. In other reported cases no form of obstruction has been discovered, and the explanation usually given is that the dilatation of the stomach is paralytic in origin through inhibition of the action of the vagi.

Both these volumes well maintain the high standard of articles which we have come to associate with "International Clinics." In addition to the subjects referred to, the various specialties, such as obstetrics, gynæcology, neurology, pædiatrics, etc., are attended to, and contributions appear from well-known men in these branches. The size and printing of the book render it convenient and pleasant for reading purposes.

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SOME DISORDERS OF THE CEREBRAL CIRCULATION AND THEIR CLINICAL MANIFESTATIONS.*

By ALFRED E. RUSSELL, M.D., F.R.C.P.,
Physician to Out-patients, St. Thomas's Hospital.

LECTURE I.

MR. PRESIDENT AND GENTLEMEN,—I have first to express my deep sense of the great honour that has been conferred upon me in appointing me to deliver the Goulstonian Lectures. When I look at the names of previous Goulstonian Lecturers I see among them those of so many distinguished physicians that I am only too sensible of the great responsibility incurred by anyone whose name is to be added to that list.

The Goulstonian Lecturer was intended to devote himself to the pathological aspect of some department of medicine. My lectures will be concerned with certain pathological changes in the cerebral circulation and with their clinical manifestations.

I will begin with diminution of the blood supply to the brain as exemplified in the ordinary fainting fit.

DIMINUTION OF THE BLOOD SUPPLY TO THE BRAIN.

Syncopal Attacks.

The fundamental factor in the pathology of a fainting fit is a diminution in the volume of blood passing through the brain. Sir William Gowers suggests that the resulting diminution of intracranial pressure may be an important factor in the loss of consciousness. The causes of an attack of fainting are numerous. It may depend on cardiac disease; it is fairly common, as would be expected, in cases of severe chlorosis and in other forms

* The 'Goulstonian Lectures,' delivered before the Royal College of Physicians.

of anæmia, with severe hæmorrhage, in conditions of exhaustion from whatever cause. We are concerned here, however, with syncopal attacks occurring apart from gross disease. Such may be precipitated by very different causes, sudden shock or excitement, the sight of a street accident, the sight of blood, a hot room, hunger and so on. Many people are very prone to such attacks, and this tendency to faint on slight provocation is apt to run in families.

Physiologically two important factors are concerned: firstly, vaso-dilatation in the splanchnic area, and secondly, cardiac inhibition. It is probable that in some cases only one of these factors is primarily concerned; in others both may be involved.

The ordinary faint is usually regarded as being a very trivial matter, so that little attention is paid to the symptoms, which are, nevertheless, of great interest. Mitchell Bruce* has epitomised them as follows:

(1) *A period preceding loss of consciousness.*—Subjective sensations are present; a feeling of sinking in the epigastrium, of giddiness; vision may be impaired; hearing is usually impaired or tinnitus is present; mentally there is a rapid fading of sensory impression.

The patient turns pale, leans against any support, eyelids tremble or close; the pulse fails, becoming weak, small and rapid; in other cases slow and irregular; vomiting may occur.

(2) *A condition characterised by insensibility.*—The muscles are relaxed, the patient falls, consciousness is completely lost, the surface is pale and possibly cold and clammy. The eyes are closed and the pupils dilated; the pulse and heart-sounds are nearly or quite imperceptible; respiration is indistinguishable or occurs as occasional weak sighs.

(3) *A period of recovery.*—Consciousness returns gradually, the pulse improves, the senses of sight and hearing can be excited, colour returns and intelligence is restored.

Some people never faint in the whole of their life; in others one isolated attack occurs; others are very prone to it on slight provocation. The emotions, such as anger, fear, joy, sorrow and horror, are among the active excitants of an attack. It is immaterial in this connection whether the mental feeling of the emotion precedes and causes the organic changes above noted, or whether the mental feeling follows on and is the result of them. Mott* has discussed this in his lectures on the "Physiology of the Emotions." The failure of the circulation is unquestionably the cause of most of the *clinical* manifestations.

Whether this sensitiveness of the cardio-vascular apparatus is due to inherent weakness in its sympathetic innervation or whether it is secondary to instability in some higher level of the nervous system is in the present connection immaterial. It is certain that many people display an instability of the vaso-motor system apart from any emotional state, although emotional disturbance may be, and often is, very evident.

S. Solis Cohen has studied this question.† He proposed the term "*vaso-motor ataxia*" for a "condition of instability of the mechanism of circulation present in certain persons, and characterised by abnormal readiness of disturbance with tardiness of restoration of the equilibrium of the cardio-vascular apparatus. The manifestations are most strikingly displayed by the heart and by the peripheral vessels of the extremities, but analogy indicates the occurrence of similar phenomena in the vessels of the glands and of the viscera, more especially in those of the kidney, of the gastro-intestinal tract, and of the brain. They may occur apparently spontaneously, but often there is a recognisable exciting cause. Among the influences acting as excitants are temperature, especially cold; toxic agents formed in the body, or introduced from without; visceral or internal reflex excitation; and emotion."

The vascular phenomena include functional heart disturbances, vaso-dilatation and vaso-constriction. Morbid alterations in the thyroid are not uncommon. He regards dermographism as an essential feature of the condition, and claims the existence of a hæmorrhagic tendency as shown by ecchymoses, petechiæ, epistaxis, hæmoptysis, hæmatemesis, hæmaturia, and retinal hæmorrhage. He enumerates a very large number of allied morbid associations, and among them hysteria, urticaria, local œdema, asthma, vertigo, migraine, epilepsy.

* 'Quain's Dictionary of Medicine,' art., "Syncope," 1894, vol. ii, p. 963.

* 'Brit. Med. Journ.,' April 4th and 11th, 1908.

† "Vaso-motor Ataxia," 'Amer. Journ. Med. Sci.,' 1894, vol. cvii, p. 130.

neurasthenia, neurotic dyspepsia, membranous enteritis, etc.

Doubtless many would hesitate to accept Solis Cohen's scheme in its entirety, but it does gather together a series of conditions, many of which are not infrequently found in combination. All are familiar with cases presenting irregular circulatory manifestations, such as blue hands, cold extremities, chilblains, palpitation, flushings, etc., often associated with migraine, neurasthenia, dyspepsia, and so forth. Such individuals are rarely robust, and in many of them, moreover, there is a marked tendency to faint on slight provocation. Solis Cohen does not include this in his large list of clinical manifestations, but vaso-motor and cardiac instability are very prominent features in many people of fainting tendencies. Their vascular mechanism is often unable to adjust itself to the slightest strain, as seen in the momentary faintness on getting up from a stooping position. The maintenance of adequate splanchnic control is a vital factor for health.

A sudden depression of the normal vaso-motor tone in the splanchnic area leads to a rapid accumulation of blood in the capacious vessels of that region. If only momentary in duration the result is merely the sudden sinking at the pit of the stomach—so common after any unexpected noise or fright. If of longer duration this preliminary sensation or aura is succeeded by a faint. The rapidity of onset of a faint depends on the nature of the cause, and is proportional to the rapidity with which the vaso-motor control of the splanchnic area is lost. Fatigue or a hot room is often associated with a very gradual development of an attack, and doubtless with a slowly increasing splanchnic change. The removal of the cause will often cut short the attack before unconsciousness supervenes. A sudden shock, however, may cause almost sudden unconsciousness, and doubtless very sudden splanchnic vaso-dilatation can occur. It is difficult to judge as to the degree and frequency with which the heart may be affected independent of the change in the splanchnic area. The feeble pulse is scarcely a criterion to go by, as it must be affected as the result of the fall in blood-pressure due to the abdominal vaso-dilatation and of the small volume of blood available for the systemic circulation. It would seem probable, however, that in some cases direct cardiac inhibition does occur. The two factors might also be brought into action simultaneously.

Attacks characterised by Cardiac and Vaso-Motor Symptoms with Modification rather than Loss of Consciousness.

Attention has been drawn of late to a type of attack in which vagal and vaso-motor symptoms are prominent and in which consciousness, though modified, is not of necessity lost.

Gowers describes a series of such cases under the title of "vagal and vaso-vagal attacks."* The vagal symptoms were chiefly sensations referred to the stomach, the respiratory system and the heart. The epigastric sensations were those of oppression, or of fulness, or were indescribable. The onset of the attacks was sudden. They were never really brief, seldom lasting less than ten minutes, more often lasting for half an hour or more. A peculiar slight mental state was common; it was generally described as a difficulty or slowness of mental operations, a difficulty in thinking or in concentrating attention. These also always began suddenly. A sense of sudden fatigue was a common initial symptom. The vaso-motor symptoms sometimes attained a high degree, coldness of skin was common, and the pulse became small at the same time. Pallor of face and shivering were common, and sometimes amounted to a definite rigor. With the coldness of the extremities tingling and numbness in them were often described, and sometimes slight tetanoid spasm occurred. Migraine was not uncommon in these cases.

In one case of a woman, æt. 28 years, the attack began with headache and inability to fix attention, followed by sleepiness. Then ensued a feeling of intense fear, extreme coldness of hands and feet and inability to move; then an indescribable epigastric sensation, and after a few minutes violent beating of the heart with a feeling of suffocation. The attack subsided as a flush developed with a feeling of warmth, perspiration and a rigor. A curious sense of unreality in all she saw was present during the attack. In severe attacks the violent action of the heart was preceded by a feeling that it had stopped.

In another case, a man, æt. 30 years, had suffered from attacks for twelve years. Quite

* 'The Borderland of Epilepsy,' p. 18, *et seq.*

suddenly a dreamy mental state would occur. This was not momentary, as in epilepsy, but persisted. With it, or just after its commencement, his hands and feet became cold, his face increasingly pale, and muscular weakness was so extreme that if he tried to sit up he fell back at once. His extremities became icily cold, even to an observer; his pulse became smaller and smaller until hardly perceptible. Consciousness was retained throughout, and he felt as if dying. This state lasted half an hour, and then he became aware that his mental state was improving, and that his feet were a little less cold. Within two or three minutes a distinct rigor set in lasting a couple of minutes, and coincident with gradually increasing warmth. He continued pale for the rest of the day. A few minutes after the rigor an urgent need for micturition was felt, and went on during the rest of the day, a large quantity of limpid urine being passed.

These symptoms may, I think, be interpreted as follows: An initial widespread cutaneous vaso-constriction is obvious. The dreamy mental state might result either from cerebral vaso-motor spasm or from a passive cerebral anæmia dependent on splanchnic vaso-dilatation. Gowers suggests that the muscular enfeeblement might be due to cerebral vaso-constriction, but it might also be aided by a vaso-constriction of the muscular area. The bulk of the blood doubtless found its way into the splanchnic area, as is suggested by the copious diuresis which occurred, and by the extreme feebleness of the pulse. The condition of the pulse further suggests that the sum total of the blood-pressure was a marked lowering, despite the cutaneous vaso-constriction, which would tend to produce a rise of blood-pressure.

In another case a woman was subject to attacks in which a sudden sense of fatigue was followed by yawning, several times repeated, and then loss of consciousness for a second or two, after which she was well—*petit mal* in fact. But she did not always thus lose consciousness; sometimes the yawning was followed by a sense of suffocation and cardiac distress, and she felt that unless she kept perfectly still she would faint. The sense of suffocation would continue for one or even two hours, but at any moment might be ended by a moment's loss of consciousness. Gowers points out that the brief attacks were clearly epileptic, but that in the longer ones prolonged vagal symptoms (respiratory and cardiac distress) were interposed "as if symptoms usually momentary as the aura of epilepsy became protracted, extended, as it were, into a vagal attack."

In another case a woman, æt. 35 years, had attacks in which a sudden intense sense of suffocation with a feeling of tightness in the head, was followed after a minute or so by a moment's complete loss of consciousness. On its return she felt cold, first and foremost in her extremities. The coldness was so intense that it made her shiver. After about ten minutes she burst into perspiration, and simultaneously her heart began to beat violently and the symptoms slowly subsided.

In this case the loss of consciousness was interposed between the initial symptoms and the vaso-motor symptoms.

I have seen four cases which may be included under the same category.

In the first case, a man, æt. 36 years, is waked up from sleep with either a violent and rapid action of the heart or a very feeble action: his extremities go icy cold; there is a sensation of tingling and tightening of the skin of trunk and extremities with free perspiration. He turns very pale, feels faint and sometimes as if dying, but never loses consciousness. With return of warmth the symptoms subside. By vigorous movements and rubbing he has sometimes arrested the course of the attack. These attacks are not uncommonly preceded by a pleasant dream. As a boy he was very liable to faint, and this tendency was noticeable in his father, brother, and two sisters. The blood-pressure varied from 110–130, but no opportunity offered of taking it in an attack. Marked constipation was present in this case, and the relief of this with a rest-cure caused an almost complete cure. The possibility of auto-intoxication is suggested by the constipation and a well-marked indican reaction in the urine. The case is very similar to Gowers' second case.

In the second, a boy, æt. 14 years, the initial symptoms consisted of a tingling of hands which spread up the arms; a tingling of feet spreading up the legs; abdominal pain, and headache. These aural symptoms may last for some minutes, and are succeeded by a fall and unconsciousness, or rather modified consciousness. The boy lies quiet, with no spasms of any sort; his face is pale, with

a grey colour round the mouth. If spoken to he is able to answer with difficulty. His mother has had three fits herself; her brother and her sister's daughter are confirmed epileptics.

In the third, a man, æt. 42 years, a sensation described as of a ball of air rising from the stomach into the throat is succeeded by a feeling of collapse and sometimes loss of consciousness (*petit mal*). Usually, however, the sensation is succeeded by a feeling of numbness of legs, which may become quite cold, and a coldness and numbness of fingers. The condition in the fingers is evidently closely allied to, if not identical with, Raynaud's disease, as they have at times become "as blue as a dark blue serge suit." This numbness and coldness of legs may last for two or three hours.

In the fourth, a man, æt. 39 years, has always been prone to ordinary fainting fits, and on one occasion he fell with absolute suddenness and without warning. In addition he has had several attacks in which he wakes up from sleep with a dizzy, swimming sensation, or with singing noises in the head. He vomits, and for a time varying up to a few hours is in a state of utter collapse and semi-consciousness. His hands and feet are always very blue and cold in cold weather.

Dr. H. G. Langwill* records two interesting cases.

The attacks in one, a woman, æt. 48 years, begin with a sinking feeling in the umbilical region and an overpowering sensation as if she were dying, consciousness, however, being always intensely alert, though the power of speaking, or even moving, is lost. The attacks come on chiefly on getting into bed. Seen in one attack she was extremely pale with a rapid pulse of markedly small volume, unable to speak, but acutely conscious of her surroundings. She was also subject to a severe "sinking feeling" constantly following upon evacuation of the bowels, so much so that she had to lie down immediately after stool.

In the second patient, a woman, æt. 38 years, the attacks also come on at bed-time with an intense feeling of "sinking," with a sensation of utter loss of all power and a feeling as if she were dying. Consciousness is always perfectly retained, face pale. For years she had always suffered on getting into bed at nights from sensations of pricking and numbness in hands and feet.

In the first case the blood-pressure was 110 and 120 on two occasions and in the second 90. On the supposition that the attacks were due to sudden dilatation of the vessels in the splanchnic region the effect of an abdominal binder with a large pad on going to bed was tried. In both cases this was extraordinarily successful.

Such cases are doubtless much commoner than is suspected, their somewhat indeterminate character and the absence of symptoms between the attacks making them difficult of recognition.

The onset is commonly sudden. The salient features are cardiac and vaso-motor with some modification of consciousness in the large majority of cases. There is obvious vaso-constriction of the cutaneous vessels in the majority of cases, as evidenced by pallor of face, coldness of extremities and tingling. Coldness of extremities was noted in eight of Gowers' eleven cases. It was present in a marked degree in two of my own. Pricking and numb feelings of hands and feet are probably also the result of vaso-constriction. They are common in the extremities in gross arterial disease.

The feeling of suffocation and the orthopnœa noticed in several of Gowers' cases are very interesting. Their nature is obscure, but it may well be that they are pulmonary in origin. The lungs contain a very capacious system of vessels, and Brodie* has shown that cardiac changes and variations in the systemic circulation can very materially alter the volume of blood contained in the pulmonary vessels. These cases exhibit obvious changes both in the cardiac and systemic systems. Vaso-dilatation in the splanchnic area is almost beyond dispute in many of the cases, although we cannot directly inspect the splanchnic vessels. The distribution of blood is disorganised over the whole body and engorgement (or anæmia) of the pulmonary vessels is very possible, and in cases in which it occurred would be a feasible explanation of the dyspnœa observed. Bronchial spasm may possibly participate in its causation.

Splanchnic dilatation is suggested directly by the disappearance of the blood from the cutaneous surface, factors of very common concurrence, and also by the copious diuresis following the attack in Gowers' second case. Rapid and rather persistent splanchnic vaso-dilatation is evidently a very im-

* "Note on the Treatment of a Type of so-called 'Fainting Attack,'" 'Edin. Med. Journ.,' August, 1908, p. 116.

* "Lectures on the Pulmonary Circulation," 'Lancet,' March 22nd, 1902.

portant factor in these cases. This view is supported by Langwill's observation of the benefit attending the use of a firm abdominal binder, a procedure, moreover, which raised the blood-pressure 20–30 mm. of mercury in his first case.

The variations in the symptoms and in order of sequence depend in my opinion on the position of the vascular area primarily involved and on the nature of the vascular crisis. An initial splanchnic vaso-dilatation with lowered blood-pressure would clearly explain some cases. A severe initial vaso-constriction, for instance in the extremities, with rise of blood-pressure may possibly occur in some cases of so-called vaso-motor angina, though Dr. James MacKenzie found that the blood-pressure was not raised in some cases he had the opportunity of examining in an attack. Sir Douglas Powell in his article on this subject in Prof. Allbutt's 'System of Medicine' notes the same cardio-vascular instability and the same physical and mental relationships. Dr. James MacKenzie discusses these abnormal circulatory disturbances under the very non-committal title of the "X Disease."* Pal has ably demonstrated the importance of vascular changes in relation to clinical symptoms in an exhaustive monograph — giving these changes the suggestive name of "Gefässkrisen"—vessel crises.

It is difficult to decide in each case whether the coldness of the skin is due to active vaso-constriction, or whether the skin vessels are merely narrowed down just enough to accommodate the diminished amount of blood available for them. On general grounds vaso-dilatation in a large vascular area which would cause lowering of blood-pressure is compensated for by active constriction in other regions. The tightening of the skin described in one case was possibly due to a contraction of the hair muscles.

Whether there is a very active vaso-constriction of the cutaneous vessels, it is clearly ineffective against the splanchnic dilatation, for it can scarcely be doubted but that the blood-pressure must usually be very low in these attacks. The pulse is usually extremely feeble. With a great accumulation of blood in the splanchnic region the pulse of necessity becomes small, and the common physiological accompaniment of a lowering of blood-pressure is an acceleration of the heart. But in some of these cases there may be active cardiac inhibition as well.

Vaso-constriction in the splanchnic region doubtless occurs at times, but it is not yet an easily recognised factor in medicine. It is probably concerned in some of the attacks known as abdominal angina. So far as this condition can be demonstrable it was shown in a case observed by Capps and Lewis.* They were aspirating a pleural effusion in a man, æt. 30 years. Blood-pressure at the commencement was 120 mm. of mercury. Two litres of serous fluid were withdrawn, the blood-pressure falling to 105. The needle then came suddenly in contact with the visceral pleura and the patient complained of dull pain in the epigastrium, but of none in the chest. The pain grew rapidly worse and the blood-pressure rose steadily to 155 in the course of five minutes. Upon withdrawal of the needle the epigastric pain gradually subsided and the blood pressure was simultaneously lowered. Twelve minutes after the maximal anginal pain the blood-pressure had returned to 108 and the pain was gone. The authors conclude that excitation of the visceral pleura had in this case caused a reflex vaso-constriction in the abdominal arteries. I mention this most valuable observation because in the present ignorance of the type of cases we are discussing it would be unwise to assume splanchnic dilatation to be invariable. The circulatory system offers abundant field for variation, and seeming contradictions may simply be due to varying phases of cardio-vascular behaviour and variations in the blood distribution.

In some of the cases consciousness has been modified—a dreamy mental state may be present, and a feeling of impending death is not uncommon. The extreme weakness of the pulse indicates a vascular depression that must of necessity affect the brain, and we know too little of the nature of mental processes to predict what alteration should attend a diminished blood flow. Momentary loss of consciousness occurs occasionally, as in some of Gowers' cases, and when it occurs he regards it as epileptic in nature, as *petit mal*. The unconsciousness may be an early or a late symptom in the attack, and in my opinion simply represents

* 'Diseases of the Heart,' 1908, p. 56.

* "Observations upon Certain Blood-pressure Lowering Reflexes that arise from Irritation of the Inflamed Pleura," 'Amer. Journ. of Med. Sci.,' 1907, vol. cxxxiv, p. 890.

the fact that when it occurs the vascular depression has reached a point incompatible with consciousness, and that this is the missing link connecting it with epilepsy. Cerebral vaso-constriction may account for it in some cases, cardiac inhibition and low blood-pressure in others.

Further the prolonged symptoms in these cases are often of a type which, if of momentary duration, would be fairly characteristic epileptic auræ. At the same time, as has been pointed out, many of them are obviously vaso-motor or cardiac in origin, and that this is recognisable is due to the fact that they are exceedingly deliberate in onset instead of sudden. If they were of slightly shorter duration and of greater intensity the epileptic relationship of these cases would be still clearer. Finally, if the cardio-vascular changes were absolutely sudden in onset, severe in degree, and transient in duration, they would be increasingly difficult of recognition and the epileptic nature of the attack unquestioned.

Gowers, of course, recognises that many of these cases present distinctly epileptic phenomena, and remarks that "velocity is an essential element of ordinary epilepsy, but this does not preclude the possibility of deliberation in attacks not far removed from epilepsy."

The Suddenness of some Faints.

Whilst the onset of an ordinary faint is gradual, in some cases it is rapid and may be absolutely sudden. A man very subject to ordinary faints on one occasion suffered from a sudden attack. He was sitting down and feeling perfectly well when he fell absolutely suddenly and bruised his face on the ground. Gowers also remarks that those who are prone to faint become after a time liable to do so more suddenly. In such cases there can be no question as to the nature of the attack. The vascular depression responsible for the ordinary faint must have occurred with greater rapidity. The suddenness suggests that a transient and sudden cardiac inhibition occurred rather than that the attack was due to splanchnic vaso-dilatation. An isolated attack of unconsciousness sometimes with muscular spasm is not an unknown event in people showing no other signs of any tendency to faints or fits. Sudden cardiac inhibition supplies the most likely explanation of these attacks.

The Conversion of Fainting Fits into Epileptic Fits.

Gowers has recorded three cases in which repeated syncopal attacks have passed into epilepsy.* Thus:

"A girl when about 7 years old became liable to faint on any sudden start or alarm. The faints had all the character of cardiac syncope. There were pallor, coldness, and gradual loss of consciousness. After some years such faints occurred without exciting cause, and became more sudden in onset. When she was seventeen years old one of these attacks passed into a distinct epileptic fit with deviation of the head, general clonic spasm, and micturition during the attack. Others followed."

The second case was that of a woman, æt. 34 years, who "had been liable for twelve or more years to apparently true fainting attacks caused by excitement, over-fatigue, or a hot room. They began with palpitation of the heart and a sense of faintness, followed by gradual loss of consciousness, which did not become complete if she was able promptly to lie down, when she always began to recover. At the age of twenty-five years these faints changed in character. She became unconscious more suddenly, and without any exciting cause; indeed, the onset was so abrupt that she only knew she had had an attack by finding herself on the floor. Recovery was then by mental confusion, not lessening faintness, and at first she could not tell where she was."

The third patient "was a woman who became prone to faint in early girlhood, especially in hot crowded places. In these she first became pale, felt faint, and gradually lost her sight, and then, if she tried to stay where she was she lost consciousness. Usually when sight had failed with help she was able to walk out of the place. During the effort dim sight returned, and the fresh air quickly restored her. These are the typical symptoms of cardiac syncope. Such faints continued until she was thirty years of age, when she became liable to sudden brief loss of consciousness, in which she often fell and sometimes hurt herself. After these she usually slept, and could not afterwards recall what had happened between the attack and the sleep. One occurred in a room with the door locked; the noise of her fall alarmed her friends, who knocked at the door. She got up and opened it, then she lay down and went to sleep, but afterwards remembered nothing of the incident.

* 'The Borderland of Epilepsy,' 1907, pp. 8 and 9.

Such attacks were undoubtedly epileptic, and after they began she ceased to be liable to the faints. She never had a convulsive seizure, but the attacks continued until she came under treatment at forty-two years of age, when they were arrested by bromide. She has since continued free. There was no heart disease and no family history of epilepsy, and no cause could be ascertained except the apparently disposing influence of the cardiac faints."

In all three cases the same phenomena were presented, attacks originally brought on by external influences and typically syncopal after a lapse of time appearing spontaneously and with a more sudden onset—in fact becoming undoubtedly epileptic.

The explanation of this change that naturally suggests itself is that the increased suddenness of the attacks is due to an increase in the rapidity with which the circulatory changes are brought about.

The symptoms of syncope are certainly due to cardio-vascular changes with alteration in the cerebral circulation, and an increase in the velocity of change would fully account for the suddenness of the unconsciousness. Gowers, however, postulates a change in the nerve elements of the brain as underlying the loss of consciousness in syncope, produced not directly by the failure of the circulation but rather by a sudden diminution in the intra-cranial pressure resulting from the circulatory failure.

He also states that "we have to conceive it" (*i. e.* a change in the nerve elements) "as occurring spontaneously in epilepsy and as due to a sudden diminution in the intra-cranial pressure in syncope," and further that these cases in which repeated syncope seems to pass into minor epilepsy "suggest that the state of the nerve elements that underlies the loss of consciousness in syncope may, by repeated induction, acquire a tendency to spontaneous development, which constitutes minor epilepsy."

I submit that by frequent repetition the "resistance" of the nervous mechanism of the cardio-vascular apparatus is diminished, the reflex becomes easier and the failure of circulation occurs with greater rapidity, with the result that the loss of consciousness is proportionately more sudden. The distinction is one of the greatest importance, for the one view assumes a suddenly developing, mysterious state of the nervous system in which it becomes liable to sudden causeless failures of its activity, causeless in the sense that they are now independent of the circulatory failure admittedly producing the earliar attacks, whilst the other view affords an explanation of these attacks more in accordance with their clinical history.

(*To be concluded.*)

August 30th, 1909.

THE NATURE AND TREATMENT OF SURGICAL SHOCK.*

By JOHN D. MALCOLM, F.R.C.S.Edin.,
Surgeon to the Samaritan Free Hospital.

I SHALL discuss only that form of shock which is induced by such a continuous injury as may be inflicted in the course of a surgical operation, and only the vascular changes which occur.

The Nature of Shock.

In recent years the most popular theory of the nature of shock has been that it depends upon an exhaustion or paralysis of the vaso-motor centres. This view was published in 1899 by Dr. George W. Crile, who asserted that both before and after death from shock "the arteries were quite empty, the tissues pale, but the venous trunks were full, alike in the somatic and in the splanchnic areas. There was a manifest transference of the blood from the arteries and capillaries to the veins."† When the splanchnic area was not involved in the manipulations of an experiment, autopsies "did not reveal a condition of vascular distension in this area different from that of other areas."‡

Advocating the same theory, Mr. Lockhart Mummery has recently said that, as shock developed, "all the small arteries could be seen to relax and become filled with blood,"§ and, writing in association with Mr. W. Legge Symes, he asserted that shock may be induced "by total destruction of the central nervous system."‖

It is not possible that the arteries can, at the same time, be "quite empty" and "seen to relax and become filled with blood," and therefore these two descriptions of vascular changes cannot refer to the same condition. Mummery's statement is the more consistent and easily understood as the result of vaso-motor paralysis. But the theory is Crile's, and observations upon pithed animals may not be accepted as evidence regarding the changes that take place in shock unless Crile's teaching

* Delivered before the Medical Society of London.

† 'Surgical Shock,' by Geo. W. Crile, p. 140.

‡ *Loc. cit.*, p. 139.

§ 'Med.-Chir. Trans.,' 1907, p. 578.

‖ 'Brit. Med. Journ.,' 1908, vol. ii, p. 787.

that the arteries are quite empty and the tissues are pale is set aside.

At a meeting of this Society sixteen years ago I asserted that there is no congestion of the splanchnic area in the state of profound shock. I then noted that, in the course of operations upon the abdomen, if the severity of the procedure endangered the patient's life the peritoneum became more and more pale. This is in full agreement with Crile's statement above quoted, but I suggested, and from time to time have ventured to maintain,* that in the state of shock there is an intense stimulus to contraction of the vascular system generally.

Recent experimental work affords strong support to this view. Dr. W. T. Porter,† jointly with H. K. Marks, T. B. Swift, jun., and W. C. Quinby, of the Harvard Medical School, has shown that in deep shock the vaso-motor centres were "not paralysed or inhibited"‡ Porter found that even when a very low blood-pressure was produced by methods leading to a condition which "surgeons would call shock," the pressure was still raised and lowered by stimulation of pressor and depressor nerves respectively. He added that the data presented by him "were wholly opposed to the hypothesis that would explain surgical shock by the exhaustion of the vaso-motor centres."§ Dr. M. G. Seelig and Dr. E. P. Lyon,‖ of St. Louis, Mo., have also shown that section of the sciatic nerve increased the flow of blood through the leg of an animal in profound shock, which clearly proved that the peripheral circulation was under the control of the central nervous system. The experiments of these gentlemen showed, further, that the flow was increased proportionately to a greater extent by section of the sciatic in the shocked than in the unshocked animal, which indicated that the vessels were contracted in the state of shock. The same observers, with Dr. John Green, jun., recorded that the retinal arteries became reduced in size, and in some cases were so small as to appear like mere threads as a result of severe injuries.

Thus the most recent experimental evidence makes the theory that the vaso-motor centres are paralysed in shock altogether untenable, and in my opinion the facts recorded by Crile do not support his conclusion.

An essential part of his argument was that a low blood-pressure in the carotid must be due to relaxation of some portion of the vascular system.* But he recorded also that the blood-pressure was raised in the splenic vein, and it was not considered which was the more important indication of the state of the vessels.

If, as Crile says,† a feeble heart action is not the chief cause of low pressure and if the quantity of blood is unaltered, an active contraction of the arteries probably invariably induces a rise of blood-pressure and their relaxation brings about a fall *in the large arteries*, but these results certainly do not follow in such small arteries as the radial. The statement that a fall of blood-pressure must be due to vascular relaxation would be true if the blood were stationary. The law that pressure upon a fluid is transmitted with equal force to every part of its surface is applicable under all circumstances to *fluids at rest*. There is no such law with regard to fluids in motion. This fact does not seem to be very generally remembered, but anyone may readily convince himself of its truth by observing an ordinary water tap, when the water is flowing freely; if the stop-cock is slowly turned pressure is made upon the stream of water, and the pressure of water beyond the tap is reduced whilst that in the direction from which the fluid comes is raised. The tube exhibited, and shown diagrammatically in the figure, consists of a number of stop-cocks arranged alternately with short pieces of iron piping, glass pressure-gauges being inserted into each of the latter. The calibre of the tube is greater at one end and narrows towards the other. This is not intended to represent an artery, but merely to show the effect of contracting a tube upon the pressure of a fluid flowing through it. It is the obstruction to the flow that causes changes in the pressure, and the effect of consecutive contractions may be exhibited.

When the distal stop-cocks A and B are closed

* 'Med. Soc. Trans.,' 1893; 'Lancet,' August 26th, 1905; 'Brit. Med. Journ.,' December 9th, 1905; 'Med.-Chir. Trans.,' 1907.

† 'Amer. Journ. of Phys.,' 1807-8, pp. 399, 444, 500.

‡ *Loc. cit.*, p. 447.

§ *Loc. cit.*, p. 405.

‖ 'Journ. of Amer. Med. Assoc.,' January 8th, 1909, pp. 45-48.

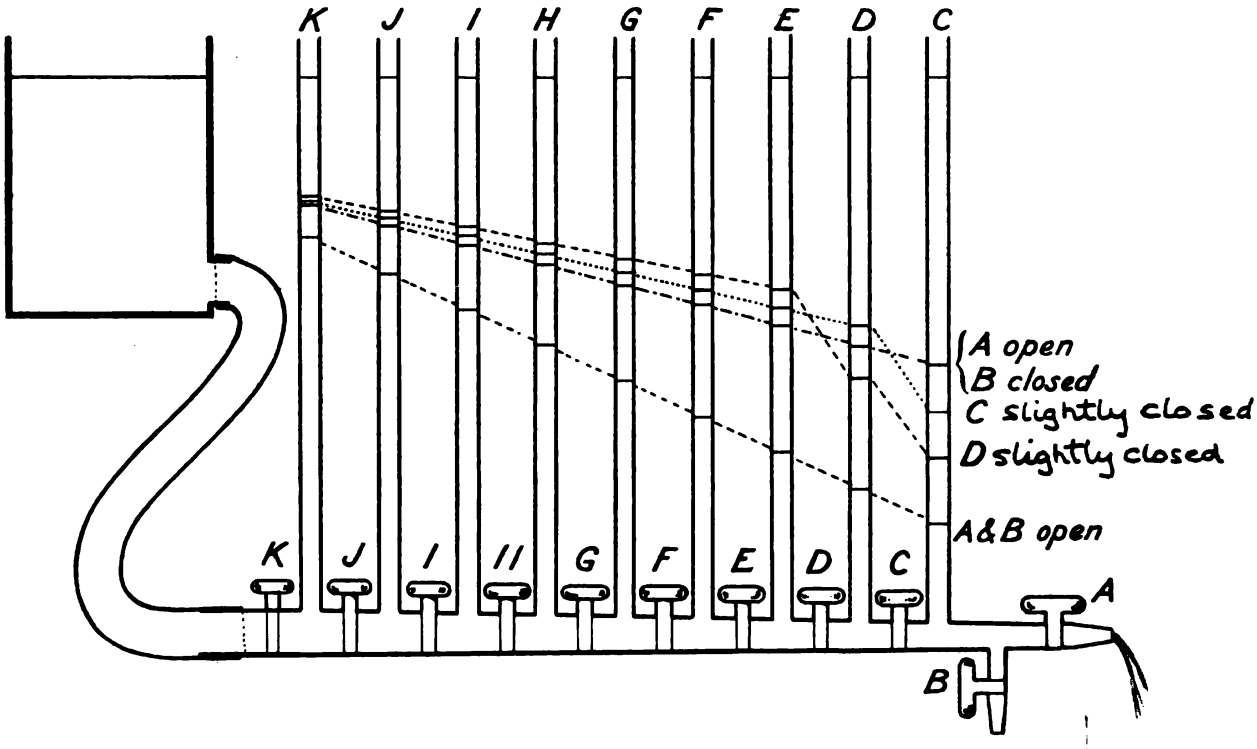
* 'Blood-Pressure in Surgery,' p. 401.

† 'Surgical Shock,' p. 153.

and the others are open the water in the gauges of course rises as high as in the cistern. When all the stop-cocks except that marked B are open, and when the tube is horizontal, the pressure of water flowing through it gradually falls as the stream passes further away from the propelling power. If the calibre at A is so arranged that the pressure is indicated by the line marked "A open B closed" then by opening the stop-cock B, the pressure is lowered througout the tube to a height varying with the calibre at B, and indicated by the line "A and B open." If B is again closed the water returns to its former position, assuming the height of water in the cistern to be constant. But the pressure may also be lowered by obstructing the flow through the tube. By turning off the taps C, D, E, etc., beginning with C and manipulating them consecutively the pressure is made to rise between each tap as it is turned, and the head of water and the pressure is lowered further down the stream, as indicated by the lines marked "C slightly closed," and "D slightly closed."

The force of gravity alters matters somewhat when the tube is not horizontal, but when that force is eliminated this lowering of pressure may be brought about in all parts of the tube, and thus the pressure may be reduced to the same or to a lower level than by opening the stop-cock B. The flow of water is retarded by the obstructions and facilitated by their removal. It follows that, by re-opening the stop-cocks C, D, E, etc., the pressures are brought back to their former levels.

If the gauges were taken away and the stop-cocks were put very close together, the effects on the pressure would not be different. If the stop-cocks were replaced by rings which could be contracted, and were made so narrow and put so close together that they would represent the circular fibres of the muscular coat of an artery, the changes induced by contracting and relaxing the rings would still be the same as these that may be shown in the tube exhibited; hence these changes faithfully indicate the alterations of pressure that would be produced by such a contraction as occurs in an artery, if no other circumstances were taken into consideration.



From this it is clear that the fact that the blood flows has to be considered in estimating the causes of changes of blood-pressure quite as much as the fact that the blood is in an enclosed space, and it is not at all certain that a fall of blood-pressure in a particular vessel is necessarily due to a general vascular relaxation. On the contrary, the presumption really is that, as long as fluid flows through it,

contraction of a tube or blood-vessel will lower the pressure of the fluid within it, if other circumstances are unaltered.

Moreover, it is altogether impossible to show a fall of pressure in any part of the tube sketched by opening any of the taps without causing a more free flow of fluid from its open end. If we apply this fact to the conditions in the blood-vessels, we must conclude that a lowering of pressure in the arteries caused by vascular relaxation should be accompanied by an increased flow of blood into the capillaries, which certainly does not occur in shock.

The fact that narrowing a tube when other circumstances are unchanged lowers the pressure of a fluid flowing through it may be demonstrated, but this was altogether ignored—was not even mentioned—by Crile as yielding a possible explanation of a fall of blood-pressure, and when I stated in previous papers that a sufficient contraction of the arteries would lower blood-pressure in the contracted vessels I was met with the assertion that "the pressure of a fluid in the nozzle of a tube is certainly not less than the pressure in the tube itself."* I have also been assured that when fluid flows through a tube of uneven diameter "the pressure varies inversely with the square of the diameter," that is to say, the pressure is higher in the narrow part in proportion to its narrowness. Neither of these statements can be verified by means of the tube on the table, and when applied to the arteries they would indicate that the blood-pressure in the arterioles is at least as high as, or far higher than, that in the aorta, which conditions have not hitherto been described. The second statement appears to arise from a confusion between pressure and velocity. There is a law that the velocity of a fluid in a tube varies inversely with the square of the diameter of the tube, but velocity and pressure are not the same. With regard to the assertion that the pressure in the nozzle of a tube is not less than that in the tube itself, as long as fluid flows out of a nozzle, if the influence of gravity is eliminated, the pressure must fall from point to point along the tube and nozzle, being highest where the force is applied and lowest at the exit of the nozzle. This is essential because it is the *difference of pressure* that makes the fluid flow. An equal pressure at two points would arrest the flow.

* 'Lancet,' 1907, vol. i, p. 1187.

As in the metal tube so in the vascular system, if the influence of gravity is eliminated, blood-pressure falls from the beginning of the aorta throughout the arteries, capillaries and veins back to the right auricle,* and changes of calibre in the vessels must influence the pressure within them in the way illustrated in the metal tube. In a former paper I recorded that in a number of cases, after an operation, hardly any pulse was felt at the wrist, but there was a strong beat in the carotids and a slow heart action. In my opinion, these conditions can be explained only if a tense contraction of the smaller arteries and a powerful heart-beat existed. If we take the flow of water through the metal tube as a guide, it is obvious that the pressure in the veins should be lowered by arterial contraction, because they are farther away from the propelling power. But the fact that the blood is in an enclosed space makes a difference. When contraction of the vessels occurs the blood must go somewhere. Naturally it accumulates in the weakest part of the vascular system, that is to say in the large veins, and thus the distension and rise of pressure in them is explained. The blood-pressure, of course, never rises as high in the veins as that in the arteries so long as the blood is flowing.

It remains to be shown how the pressure in the large arteries, which is at first raised, may eventually be lowered by an active contraction of the arteries. It has long been known that peripheral irritation causes vascular contraction, and in 1893 I quoted Professor Roy and Mr. Adami to the effect that the heart as well as the vessels is stimulated to increased effort by irritation of sensory nerves.† There is no evidence that the increased effort thus induced is not proportional to the degree of stimulation, and Dr. Eugene Boise,‡ of Grand Rapids, Michigan, has advocated the view that a strong, almost spasmodic effort of the heart and arteries is the principal feature of the vascular changes of shock. He, also, pointed out that Crile described the veins in that state as full, tense, and even enormously engorged, and yet explained the low blood-pressure in the carotids by the assertion

* 'Starling's Physiology,' p. 197. The pressure is of course per unit of surface.

† 'Philos. Trans.,' vol. clxxxiii, 1892, B., pp. 256, 257.

‡ 'Amer. Journ. of Obstet.,' 1907; American Gynæcological Society, 1908.

that the heart cannot receive sufficient blood *because the tension in the veins is low.* Boise shows that the range of ventricular dilatation in diastole is much reduced in shock, and to this he attributes the diminished intake and output of the heart, the lowered blood-pressure in the arteries, and the accumulation of blood in the veins. This view is supported by the fact put forward by Crile, that, if the stellate ganglia are removed, the heart's action remains slow, its dilatations are ample, the carotid pressure does not readily fall, and death is delayed in circumstances which, with the nervous system intact, would induce a quick pulse, a low blood-pressure in the carotid, and rapid death.

If the vessels and heart are stimulated to increased effort by traumatism, the first effect must always be, as shown by Porter, a rise of blood-pressure in the large arteries. Crile has also shown that there is a rise of pressure in the veins when shock develops. As a result of these changes, serum will be expressed into the tissues, and the specific gravity of the blood must rise. The total volume of the blood is necessarily diminished by loss of its serum, and later there can be little doubt that all its constituents are removed. I will show presently that there is abundant reason for believing that the volume of the blood is diminished in shock, and that much fluid is removed not only from the vessels, but also from the body. If these processes continue long enough, the loss of blood must be a powerful factor in the reduction of blood pressure.

Thus all the vascular phenomena of surgical shock, the lower blood-pressure in the arteries, the raised pressure in the veins, the pallor, the shrivelled, shrunken appearance, the small and rapid pulse and the sweating, are fully accounted for as the effects of an intense vascular contraction. The extreme lassitude and the dazed condition may be explained by the shutting off of the blood supply from the nervous centres, but it is not asserted that the vessels only are affected in shock. Paralysis, or excision of the vaso-motor centres, gives rise to quite a different set of conditions.

By the explanation given by Boise, the very common belief that the heart's action is ineffective in shock, because of cardiac weakness, is completely harmonised with the view that the vascular system is stimulated to a tense contraction. I am not inclined to agree that the heart change is primary to the vascular change. I think the vascular change is primary, because, as in the cases I have mentioned, it may occur alone, but as a rule the quick heart action develops so rapidly that it can hardly be called secondary.

The Treatment of Shock.

Both from a clinical and from an experimental point of view it is important to remember that whatever the changes in the vascular system may be as shock develops, opposite changes leading directly or indirectly back to the normal must take place during recovery. Moreover, recovery tends to begin as soon as traumatism ceases, and therefore care is necessary to avoid confusing the two stages.

As I understand Crile's teaching he would have us believe that the vessels become relaxed as shock develops, that the quantity of blood is therefore insufficient, and that fluid should be given to increase its bulk. My view is that the vessels become so firmly contracted because of traumatism that fluid is removed from them. It is also removed from the body, and when vascular relaxation occurs the amount of blood is deficient. Hence the patient cannot recover from a state of severe shock until fluid is administered. The evidence in favour of this last view is exceedingly strong, and Crile furnishes perhaps the strongest part of it. He says that "In every observation upon animals in shock saline solution caused a rise in the blood-pressure, . . . in the cases of moderate shock the gain was fairly well sustained, . . . in the cases of deepest shock the rise of blood-pressure was not sustained beyond a certain time even during the infusion, . . . blood-counts and hæmoglobin estimations showed that the blood was not much diluted by the saline. The solution escaped from the vessels at a rate fairly proportional to the rate of infusion, . . . the fluid accumulated in the wall and the lumen of the stomach, the intestines and the abdominal cavity—in the respiratory tract, the thoracic cavity and the subcutaneous tissue.

"When the infusion approximately equalled 320 c.c. per kilo, the amount of fluid accumulated in the splanchnic area caused embarrassment, even failure, of respiration by mechanically fixing the diaphragm and the moving ribs."*

* 'Blood-Pressure in Surgery,' pp. 269–270. It is possible that the escape of fluid into the tissues of a dog

Mummery has confirmed these observations* and I am unable to discover by what reasoning they can be brought into harmony with Crile's theory. If, as he teaches, the vessels are relaxed, they should be capable of accommodating more fluid in proportion to the degree of shock. But Crile's statement is quite clear that the vessels, including the "empty" arteries, accommodate less fluid in proportion to the depth of the shock. Under the circumstances described an attempt to distend the vessels would seem to be not only useless, but also a cause of new dangers.

The clinical evidence that the vessels contract in shock is also emphatic. It was formerly the rule after operations upon the abdomen that little or no fluid should be given to the patients. Under that treatment they sometimes remained in a state of dangerous shock for many hours. The contrast between convalescence then and now is very remarkable. We know now that in cases of uncomplicated shock the administration of fluid when the operation is finished has an immediate beneficial effect.

But there is no evidence that the dilated vessels become over-filled when shock is treated by injection of fluids. On the contrary, it is obvious that as a patient recovers from an operation, whether fluids are given or not the vascular system returns more or less quickly to its normal state. As the administration of fluid is essential to rapid recovery, it seems to me incontrovertible that when the state of shock is being induced fluid is lost by the body in quantities roughly proportionate to the degree of shock and that this loss has to be made good.

The removal of fluid, which is probably chiefly effected by perspiration, is so rapid that the symptoms of shock have been described as the symptoms of hæmorrhage, and we all know that a considerable loss of blood in the course of a severe operation is one of the most powerful aggravating causes of shock. It would seem, therefore, that although fluids are removed rapidly, yet some difficulty in the disintegration and escape of blood is an important factor in preventing a still more rapid development of shock. An attempt to keep the vessels distended by injecting saline fluid has been shown by Crile to be practically useless and dangerous when relief is most urgently required. An injection of blood, if practicable, would be more effectual because it would be less easily expressed from the vessels, and the effects of blood-transfusion upon the important parts of the body may be obtained to some extent by elevating and bandaging the limbs, by pressure upon the abdomen, and by the pressure upon the greater part of the body which may be obtained by means of the rubber suit invented by Crile.

But these methods are directed to oppose changes which progress in spite of treatment if the cause continues with sufficient force, and real benefit is only obtained when the traumatism becomes less severe or ceases. It is, therefore, important to reduce manipulation as much as possible, and to finish the operation as quickly as is consistent with its proper performance when symptoms of shock are recognised.

If the patient recovers, as soon as the stage passes in which fluid cannot be retained in the vessels—that is to say, in my opinion, as soon as the tendency to contraction abates—fluids are necessary to fill up the vessels, and their administration is most urgently required immediately after vascular relaxation begins, because then the amount of fluid in the body is smallest, and when the vessels begin to relax the disproportion between the capacity of the vascular system and the amount of the blood is more important than it is when the fluid lost has been partially replaced. The patient, at the end of a severe operation, if in a condition of shock, actually is suffering from the effects of loss of blood, even although there may have been little or no hæmorrhage during the necessary manipulations. At the beginning of convalescence, when all fluids were rigidly withheld, it was a common observation that patients were apt to collapse on being moved from the operating table to bed. Probably at this time the blood-pressure falls lower than at any other, and the venous system also should show a low pressure. Hence it is desirable to introduce fluid even before recovery begins—to anticipate the necessity for it—and the dangers of forcing fluid into a vein may be avoided by injecting it into areolar tissue—the rectum or the peritoneal cavity. It has been said that in shock drugs administered hypodermically

in the circumstances detailed is greater than it would be in a man, because a dog exudes excess of fluid so much more by the lungs and mouth, and this exhalation may be interfered with by the anæsthetic and other arrangements.

* 'Brit. Med. Journ.,' 1908, vol. ii, p. 786.

enter slowly, if at all, into the blood-stream until the condition which they are designed to treat is passing off.* But when fluid cannot be absorbed in these ways, the evidence shows that if it is injected into a vein it will be at once transferred to the tissues. When the vessels relax, a direct injection into a vein causes, of course, more immediate and striking results, and it can do no harm then if the fluid is unirritating, and not too rapidly administered. It is when the vessels are tensely contracted and still contracting that an injection into a vein may be harmful.

Under the influence of the theory that the vaso-motor centres are paralysed, certain other forms of treatment have been advocated which seem to be directly contra-indicated if experimental records are taken as a guide. For example, in deep shock, when the arteries are, as described by Crile, empty, and when, as Crile and Mummery say, saline fluid injected into a vein is rapidly transferred to the tissues, the administration of a strong vaso-constrictor like adrenalin, which must be given with a large quantity of fluid, seems an altogether irrational procedure. It is now well known that the injection of adrenalin into areolar tissue has, in a number of cases, been followed by extensive sloughing of the skin. This is an easily explained effect of a powerful vaso-constrictor upon tissues in which the arteries are contracted. or are relaxed but empty. Crile declared that "great caution must be exercised in the administration of adrenalin. Its practicality has not yet been established,"† and Mummery has recently stated that treatment by this drug is useless ‡ Hence the subject need not have been mentioned here but for the fact that other vaso-constrictors have been suggested as being probably useful. I would therefore express, as strongly as possible, the opinion that the administration of any vaso-constrictor is calculated to do harm rather than good as a treatment for developing shock.

Again, it has been said that there is danger of drawing blood to the surface and increasing perspiration if we try to maintain the patient's normal temperature by artificial heat. But Crile asserted that in winter, when the heating apparatus of his laboratory was temporarily out of order, animals "seemed to succumb more readily than under the ordinary warmth."* Clinically the question hardly seems to bear discussion. When a patient's skin is cold, when his expired breath is cold, when his internal and superficial temperatures are both falling, and when we are informed that animals experimented upon die more readily if they are not kept warm, there can, in my opinion, be no doubt that every reasonable effort should be made to maintain the temperature of the body by artificial means. It is, of course, well known that sweating is not directly dependent upon the blood supply of the skin, for it may be excited in a dead cat, and the slightest evidence of a return of blood to the surface is clinically an important indication that the patient's condition is improving.

The use of alcohol has been condemned by Crile and his followers, because it relaxes the vessels, but it seems to me that when we desire to fill up the vessels and cannot do so, the proper treatment is to give sedatives, anti-spasmodics and vaso-dilators, and to apply heat and friction.

Boise† advocates the use of a preparation of veratrum viride in solution. He teaches that this drug lowers the blood-pressure in the normal animal by relaxing the vascular system, and raises it in the animal in the state of shock by diminishing excessive cardiac and vascular efforts. This contrary effect of treatment in the two states is important. It is well seen also when alcohol is given. Mummery records that in shock after the administration of alcohol the pulse is often "much more easily felt, and one is led to suppose that the blood-pressure has been raised." He argued that in health alcohol lowers the blood-pressure, and therefore "that the apparent improvement in the pulse is due to vaso-dilatation and an increased flow through the vessels."‡ This explanation is clearly the correct one, but it does not in my opinion make the improvement "apparent" in the sense of being unreal, and it is difficult to understand how a dilatation and increased flow can occur in vessels which are described as already relaxed and filled with blood.

I do not think it is possible to explain satisfactorily the action of alcohol if the vaso-motor centres are regarded as paralysed in shock. But the

* 'Brit. Med. Journ.,' vol. ii, 1908, p. 788.
† 'Blood-pressure in Surgery,' p. 409.
‡ 'Proc. Roy. Soc. Med.,' April, 1909, p. 66.

* 'Surgical Shock,' p. 136.
† *Loc. cit.*
‡ 'Lancet,' 1905, vol. i, p. 780.

improvement brought about by its administration is often very obvious, and the facts are easily and fully accounted for if the vessels are regarded as contracted. In the tube exhibited I have already shown that if the flow of water from A is made easier the pressure falls throughout the tube just as the blood-pressure falls when the small arteries relax under the influence of alcohol. But the pressure in the metal tube may also be lowered by contracting its lumen, and then, by re-dilating the contracted parts, the pressure is again raised. So in shock it seems to me that the blood-pressure falls in the smaller arteries because they contract, the contraction and fall of pressure extending to the larger arteries in proportion to the severity of the irritation. Then, vaso-dilators promote a return to the normal and an improvement in the radial pulse.

The giving of strychnia in the treatment of shock has been condemned because in animals under the influence of curare it produces the vascular changes of shock. Crile injected curare into dogs in sufficient quantity to prevent convulsions. Then strychnia was injected in doses that would induce convulsions but for the action of the curare. A rise of blood-pressure followed and sometimes continued one and a half hours. Every subsequent dose caused a rise of less extent and duration, and every rise was followed by a greater fall until the low carotid blood-pressure of shock was developed and burning the paw had no effect on the pressure. From this it seems clear that strychnia contracts the blood-vessels, and if I understand Crile's teaching, he says that this drug over-stimulates and exhausts the vaso-motor centres. But it has been shown that contraction of the arteries can fully account for the vascular changes of shock. Crile did not mention that the contraction of the vessels caused by strychnia might act in this way, although it seems to me that he proved that the constricting action of strychnia persists until the vessels can contract no more, just as Porter showed that stimulation of a pressor nerve contracts the arteries until life cannot be sustained if there is a further contraction. The question for settlement is whether strychnia causes vaso-motor exhaustion or excessive vaso-motor irritability. That curare prevents the development of the usual obvious manifestations of strychnia poisoning is easily understood, but that strychnia causes paralysis of any function of the spinal cord is improbable, and is certainly not proved.

Indeed, the fact that strychnia produces the vascular changes of shock when the development of convulsions is prevented, seems to me to afford very strong evidence that in shock the vessels are powerfully stimulated to contract.

Notwithstanding the fact that large doses of strychnia cause the vascular changes of shock, its administration in small doses may be beneficial as treatment of this condition. In 1853, Brown Sequard* taught that strychnia does not act directly upon the spinal cord, but by causing an increase of nutrition of the nervous centres. If, as I believe, in shock the shutting off of the blood supply from the nervous centres is the final cause of death, an action of strychnia tending to increase the nutrition of these centres would obtain for it a firm physiological basis as a drug calculated to prove useful in the treatment of shock.

I do not propose to discuss the influence of anæsthetics, but one of the most important factors in preventing shock is the improvement in recent years in the methods of their administration and of securing a proper ventilation and oxygenation of the blood. Formerly patients were sometimes well advanced towards a state resembling that of deep shock before an operation was begun, and surgeons cannot too fully acknowledge their debt to the anæsthetist in this respect. The disuse of irritating antiseptics has also had a beneficial effect by reducing the irritation of the tissues, and in pelvic surgery the Trendelenberg position is an important preventive of shock. The advantages of the head-down position in an emergency are of course well known.

Improved methods are so efficient in preventing the development of shock that with a free administration of saline fluid the surgeon now sees comparatively little of this condition in normal patients.

But the degree of shock depends upon the degree of injury, and the effect of injury depends upon the resisting power of the patient. It is when the patient is very weak, and more particularly when he is in a septic condition, that the dangers of shock are usually most urgent. One of the greatest factors in reducing our experience of shock is the improved diagnosis which enables us to operate before septic, febrile and extremely debilitated conditions arise.

When a surgeon is compelled to operate upon a patient in a septic condition, the vascular system is already, before the operation begins, well advanced towards the state it assumes in shock

* 'Experimental Researches applied to Physiology and Pathology,' E. Brown Sequard, 1853, p. 63.

and the danger is correspondingly increased. I believe the explanation of the pulse conditions in the two cases is the same, and there is no doubt that the pulse of a patient dying of septicæmia and that of one in deep shock are very much alike.

The septic patient has indirectly lost much blood, chiefly by continuous sweating. Hence fluid to such a patient is a food which is never more necessary than when a severe or prolonged injury is being inflicted. It is well known that fluid is required in cases of starvation and exhaustion sooner than solid food—that is to say, life can be maintained longer on fluids than on solids alone. Injections of saline solution are therefore useful in the cases under consideration simply to replace the fluid which is constantly being lost, quite apart from any need for filling up or dilating empty vessels. If fluid is given as a food during an operation upon a septic patient, the additional advantage is gained that as soon as the vessels relax at the end of an operation, or when traumatism is diminished in the course of it, fluid is at once available to fill up the relaxing vessels. No advantage is obtained by injecting the saline solution into the veins for this purpose. The treatment is safer and equally efficacious if the injection is made, of course with careful precautions against sepsis, into loose connective tissue. This method may be employed with advantage in the case of a very weak or septic patient even before the operation is begun.

The treatment of septic peritonitis by continuous rectal injections is intimately associated with the treatment of shock. It has been said that by this means some vital current is reversed and the peritoneal cavity is directly washed out. But when such washing out of the peritoneum can take place, an operation is necessarily accompanied by peritoneal drainage, and, if the patient does well, the discharge is copious for from twelve to thirty or more hours after the incisions are made. This copious discharge exhausts the fluids of the body just as they are removed rapidly when shock develops, and shock combined with such free drainage necessitates much and prolonged imbibition of fluid if recovery is to take place. If fluid is not supplied the discharge ceases or the vessels become empty, and in either case the facilities for the development of septic germs are increased and recovery is delayed or prevented altogether.

Hence in these cases a prolonged administration of fluid helps to fill up the vessels which relax as shock is recovered from, and also to replace the fluid lost by the profuse serous discharge.

Summary.

To sum up: I would urge that the true explanation of the vascular changes of shock is the simple and straightforward one that they depend upon an exaggeration of the physiological action by which stimulation of sensory nerves causes increased vascular and cardiac muscular efforts. This at once raises blood-pressure in the large arteries and lowers it in the small arteries. The lowering extends to the larger vessels in proportion to the degree of irritation. The heart is at first increased in power. Later it becomes relatively weak and its pace hastens. Its relaxation in diastole becomes so limited that it cannot take from the veins a normal quantity of blood and its output is therefore diminished; consequently the venous system becomes engorged, serum escapes from the vessels and from the body, and, if the action is sufficiently prolonged and severe, blood is almost certainly destroyed as in a fever. Thus the amount of blood in the body is diminished, and in fatal cases death is caused by a shutting-off of the blood-supply from the nervous centres. If recovery occurs, when vascular relaxation takes place there is a marked disproportion between the diminished quantity of the blood and the vascular capacity, and therefore there is much danger from the collapse frequently observed in conditions of anæmia.

The view I oppose is founded upon an extensive, most interesting and most instructive series of experiments, but I believe the evidence has been altogether misinterpreted. This opinion is supported by the fact that other writers who have advocated Crile's theory have advanced statements in its favour which cannot be reconciled with his. Moreover, the theory is constantly at variance with its author's own assertions, and it has been shown by positive experimental evidence that the vaso-motor centres are *not* paralysed even in the deepest degrees of shock.

If my view is right, treatment should be directed to relaxing the vessels as shock develops and to filling them up as soon as relaxation begins. Vaso-constrictors should not be given, and attempts to rapidly and forcibly dilate the vessels should not be made. Vaso-dilators are indicated, but these may induce an even more dangerous condition if fluids are not at the same time supplied to fill the relaxing vessels. Complete quietude, especially in the early stages of recovery, is necessary to prevent collapse, and, of course, the patient should be kept warm and recovery from the anæsthetic must be attended to. The patient should not be drained of fluid by preliminary treatment, but, when time is available, this does not preclude attention to the condition of the alimentary canal, an overloaded state of which is so undesirable. All causes of weakness should be obviated as much as possible and septic conditions should be anticipated by every means in our power. An operation upon a septic patient should be performed quickly, and its scope should be limited to the procedures which are absolutely necessary for his efficient relief.

August 30th, 1909.

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* *Specially reported for the Clinical Journal. Revised by the Author.*

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A CLINICAL LECTURE

ON

PUERPERAL SEPTICÆMIA AND ITS MODERN TREATMENT.

By G. BELLINGHAM SMITH, M.B., B.S.Lond., F.R.C.S.Eng., and

J. W. EYRE, M.D., M.S.Durh., D.P.H., F.R.S.Ed.

THE subject is rather a wide one, a most important one, and most distressing to all concerned; moreover it raises many difficult questions as regards diagnosis and treatment.

When we see a patient suffering from puerperal fever the first thing we ask ourselves is this: Is the general condition one of sapræmia or septicæmia? And by these terms we usually understand something like the following: that *sapræmia* is a condition produced by the absorption of toxins due to the growth of putrefactive organisms on retained clot, or products of conception in the uterus. The condition is not usually ushered in by a rigor, and the general condition is less severe than in septicæmia. The lochia are not suppressed, but often excessive, brown coloured and always offensive. On washing out the uterus or clearing it out with the fingers we find pieces of putrid placenta or clot.* On removal of this we confidently expect a rapid recovery. That in *septicæmia* we have a very severe general condition due to the growth in the blood and tissues of a pathogenic organism. It is ushered in by rigors. There is suppression of milk and lochia. There is no foul discharge, and on examination the uterus is found to be empty. With a persistent high temperature, rapidly increasing pulse and the onset of sickness and diarrhœa, the patient steadily goes down-hill, and we know that her chances of recovery are very small. These descriptions stand for typical examples of two conditions we

meet with in puerperal fever. But in actual practice all is not such straight sailing. We meet with many difficulties with regard to diagnosis, and cannot always place our cases to our satisfaction in one group or the other. We meet with a case, for instance, in which a sharp attack of fever subsides after a few days, and in which no foul discharge has occurred, and in which nothing in the shape of retained products or clot is found in the uterus. Clinically we regard it as sapræmia, but there are no putrefactive organisms present. Or, again, we have a case with a foul discharge, and we remove from the uterus offensive clot or products of conception. Instead of the rapid recovery we expect the case goes from bad to worse and eventually dies.

Practically, as we all know, we are in a difficulty whenever fever occurs after a confinement. Is there, after all, something wrong with our theoretical conceptions of the different varieties? Are they as cut and dried as ordinary descriptions would lead us to believe? A day or two ago I picked up a text-book on obstetrics—one of the best I know of—and there I found the definitions as I have already described them: that *sapræmia* is a condition of intoxication due to the absorption of poisons produced by putrefactive decomposition. But I found as illustration of a severe condition of sapræmia, producing a so-called "putrid endometritis," the picture of a uterine wall infiltrated with *Bacillus coli communis* (a pathogenic organism), and further, I read the statement that in such severe forms of sapræmia a careful bacteriological examination will show, in probably every case, the presence of pathogenic germs in addition to the saprophytes. Now, either the definition of sapræmia is wrong or such cases ought not to be included under this heading, for here we see it frankly stated—and we know it to be the case—that in addition to the putrefactive organisms pathogenic organisms are often present. And this, I think, is the first point to insist on: *that any view which defines sapræmia as due to the growth of putrefactive organisms alone is incomplete.*

As a matter of fact bacteriological examination has proved abundantly in cases of sapræmia that not only putrefactive organisms are to be found, but in association with them or independent of them pathogenic organisms are not uncommonly present.

It follows consequently that the term "sapræmia" should be held to include all cases of toxæmia due to the growth of organisms localised in the pelvic organs or passages, whether putrefactive or pathogenic.

Knowing these facts we cannot afford to regard lightly any *supposed* case of sapræmia, when we remember that there may be present organisms capable under favourable circumstances of getting into the circulation and causing septicæmia. We see in this a ready explanation of those cases which, after a mild course, regarded no doubt correctly as sapræmia, light up suddenly and terminate in death. One good example of this I saw a year or two back. A woman of humble circumstances had been up and about for a fortnight after her confinement, when she was taken suddenly ill with all the signs of septicæmia, from which she died. It appeared that she had had from the time of leaving her bed an offensive discharge, to which she had paid little attention.

I think it would be as well if we dropped the term "sapræmia" altogether, as it seems to have acquired by custom a significance not supported by bacteriology, and to have been raised to the rank of a substantive disease. We do not say a person has sapræmia when he has a whitlow. We know that he will suffer some constitutional disturbance without particularising it. So in the same way with pelvic infections. That the patient will have some general symptoms goes without saying, but it is not the sapræmia that is of importance, but the local condition bringing it about, whether putrefying clot or local infection of uterus or vagina with such pathogenic organisms as the streptococcus.

Finding pathogenic organisms so frequently in the discharge we should expect to find some local lesion. This may not be obvious, owing to its situation in the uterus, but very often it exists in the form of a sloughing perinæal wound or a puerperal ulcer of vagina or vulva. It is curious how often a very obvious lesion of this kind is overlooked. And this is a second point I would lay stress on: *To look carefully in all cases for a local lesion.* This is of importance from more than one point of view. It explains the nature of the case and the mode of infection, and moreover it has an important bearing on treatment, as we shall see later.

The toxæmia resulting from local infections varies very greatly in severity. It may be mild, as is usual with staphylococcal infections, but with streptococcal infections it may be very intense, suggesting septicæmia.

Bearing in mind the severity of the toxæmia that may accompany purely local lesions, the next question of importance we have to ask is this: Can we say in any case whether the general symptoms indicate toxemia only or early invasion of the blood-stream by pathogenic organisms?

I have pointed out some of the difficulties that are met with clinically.

Putting aside on the one hand those cases where this elevation of temperature is temporary or trifling in character, and on the other hand those in which the extreme severity of symptoms leaves no doubt as to the nature of the malady, we are left with a large number of cases in which, apart from bacteriological examination of the blood, it is impossible to say in the early stages—that is when diagnosis is of importance—that the blood is not the seat of growing organisms.

As regards the organisms present in cases of puerperal fever, figures of different observers, whilst agreeing as to their nature, differ a good deal as to their relative importance. On one point all agree, and that is as regards the overwhelming preponderance in severe cases of a *streptococcus*.

Of cases that die nearly all are due to streptococcal septicæmia. In the majority of severe cases that recover the streptococcus is found in the uterine and vaginal discharge. In a small proportion of severe cases the *Bacillus coli communis* is found, and though there has been considerable dispute in the past as to whether this organism exists alone as a cause of septicæmia, Dr. Eyre tells me that he knows of two cases of puerperal fever in which septicæmia was caused by this organism alone. It is often found in the vaginal discharge, sometimes alone, more often associated with other pyogenic organisms, and its presence is considered to increase the virulence of other organisms with which it is associated. Another organism occasionally met with and capable of giving rise to septicæmia is the *pneumococcus*. I had a case in hospital in which death occurred from infection by this organism. The bacteriology of the case was worked out by Dr. Eyre.

The *staphylococci* are almost always associated with mild cases of fever, and give rise as a rule to local infections.

As regards the *gonococcus*, whilst it is known to be capable of giving rise to septicæmia, neither Dr. Eyre nor myself have any experience of it as a cause of puerperal septicæmia.

Treatment.—I will now pass on to treatment, and before mentioning the subject of serum and vaccines, I will consider some points in connection with the examination and local treatment of a case of fever.

First of all, a careful local examination should be made—the perinæum for a septic wound, the vulva and vagina for puerperal ulcers or membranous vaginitis, the cervix for tears which have become septic. A purulent discharge will indicate the presence in the genital tract of some lesion due to infection with a pyogenic organism. The importance of discovering some infecting lesion in the vulva or vagina is this—that we ought to hesitate before we proceed to examine the uterus. I am satisfied that in some cases infection is introduced into the uterus from some lesion below, as the result of exploration of the uterus, which has come to be regarded almost as a routine measure. The risk of infection of the uterus is so great that unless I feel certain, as would be evidenced, say, by the obvious escape of purulent or foul brown discharge from the cervix, that the uterus is already infected, I prefer to assume that it is free from infection, and confine treatment to the vaginal or vulval conditions. I also avoid douches, contenting myself with careful swabbing of the vagina or vulva, followed by loose packing with iodoform gauze.

In cases of membranous vaginitis I think it is safe to assume that the uterus is infected also, and after cleansing the vagina the uterus may be washed out and packed with iodoform gauze.

We need have no hesitation about exploring the uterus in those cases where no obvious cause is found on careful examination of the vagina and vulva. This would be particularly indicated where an offensive brownish or red discharge points to something retained in the uterine cavity. In these cases we might try in the first instance an intra-uterine douche. But if this is not successful in about twelve hours' time in reducing the temperature, there should be no hesitation in exploring the interior and removing with the finger any material left behind. All procedures of this kind should be

as gentle as possible, and the curette should not be used. If the uterine wall is the seat of infection the curette cannot possibly remove all the infected tissue, and it will only succeed in destroying such barriers as Nature has succeeded in erecting, and in baring fresh tissue for infection. Neither should caustics or very strong antiseptics likely to have a caustic effect be employed. We have to aim at washing away the discharge rather than penetrating through necrosed tissues to the layer of organisms. The provision of drainage is effected by light packing with iodoform gauze, which should not be left in longer than twelve hours. On its removal another intra-uterine douche should be given, followed if necessary by fresh packing. Such in a few words are the lines on which local interference should be carried out in the first instance. Into the indications for treatment that may arise at a later stage I cannot go now, nor do I think it worth our while to stay to consider the routine treatment of puerperal fever by such measures as drainage of the peritoneal cavity through Douglas's pouch or removal of the uterus. Any such routine treatment I believe to be wrong in principle and likely to prove disastrous in practice.

As I have already pointed out, it is practically impossible to decide in a case of any severity whether the general condition existing is due to toxæmia or to septicæmia. Consequently the only sure method of knowing whether infection is local or general is by bacteriological examination of the blood. As illustration of the advantage of doing so and the treatment by serum and vaccines, I will shortly read the notes of two cases which have recently been under the care of Dr. Eyre and myself.

As regards serum treatment the results were for some years so disappointing that I came to regard it as useless. One reason for its failure was the difficulty of obtaining a serum prepared from the same strain of streptococcus as that causing the disease. Another reason probably was that treatment was started too late. Too much time was wasted in preliminary treatment and diagnosis.

On the introduction of a polyvalent serum—a serum prepared from several strains of streptococci—I was more hopeful of results, and it was not long before I had a case, which was clinically septicæmia, though not bacteriologically confirmed, and in which I was satisfied that the serum was an important agent in the recovery of the patient. It was not until quite recently that with Dr. Eyre, I tried the more recent treatment by vaccines. The two following cases of septicæmia show the advantages of the use both of a polyvalent serum and of vaccines, in the one case the serum quickly bringing about a fall of temperature and cessation of symptoms, in the other, which proved fatal eventually, the septicæmia disappeared as the result of vaccines.

Case 1.—The history of the first case is as follows: The patient was a young woman, a primipara, of apparently good constitution. Labour commenced on October 9th and proceeded slowly. The next day pains became more severe, and in the evening the occiput, which was found to be posterior, was rotated forwards and delivery effected with forceps with chloroform. The perinæum was torn and was sewn up with three carbolised catgut sutures. On the 11th, the day following the confinement, the temperature was 99° F. and the pulse 100. On the 12th the temperature went up to 101° F., and the breasts were tense. On the 15th the temperature was 103° F. at mid-day; the perinæal sutures were removed and the patient was douched with mercuric iodide lotion 1–2000. Later in the day the temperature rose to 105° F., and I was asked to see her. She was said to have had no sleep since the confinement. I found her (at 6 p.m.) looking extremely ill, with a running pulse of 150. There had been no sickness or diarrhœa. There was milk in the breasts, and she had continued suckling the baby. The lower part of the abdomen was a little tender, but there was no distension or dulness in the flanks. The temperature was 105° F. On examining the vulva a quantity of offensive pus was seen escaping. The perinæal wound showed no signs of healing, and was covered with a greyish membrane. I cleansed the perinæal wound and made a vaginal examination, and found in the vaginal vault, to the right of the cervix, a typical "puerperal ulcer"—a round, sharply cut ulcer the size of a shilling. There was tenderness about the vault of the vagina, but no deep induration. The cervix was closed, though the uterus was not involuting well. The membranous perinæal wound and puerperal ulcer pointed to a streptococcal infection, whilst the general condition, and more particularly the pulse of 150 and the sleeplessness, made me fear septicæmia.

The first question that arose was whether the uterus should be explored. I decided at once against this. If it were not already infected an examination of its interior would almost certainly lead to a conveyance of organisms from the vagina. If it was infected it was probably with streptococci, and the benefits to be derived from douching were more than balanced by the risk of infection, if it was as yet free from organisms. The condition pointing to streptococcal local infection and septicæmia indicated certainly the use of polyvalent serum, and 20 c.c. of this was injected. At six the following morning the temperature had fallen to 99·6° F., but was followed by a rise to 105° F. by 1 o'clock. Two more doses of the polyvalent serum of 10 c.c. each were given in the morning and evening.

To settle the bacteriology of the case and to prepare, if necessary, vaccines for injection, I asked Dr. Eyre to see the patient. He saw her the next day (16th) and took cultivations of the blood and vaginal discharge.

The following day (17th) the temperature came down to 99·4° F., and from this time on did not rise above 100° F., ranging mostly between 98·4 F. and 99·4° F. The temperature fell then within thirty-six hours from 105° F. to 99° F., after three doses of the anti-streptococcic serum. I was interested consequently to hear Dr. Eyre's report, for I should have had some hesitation in diagnosing septicæmia. He obtained from the blood a pure cultivation of streptococcus, and from the vaginal discharge a mixture of streptococcus and *Bacillus coli*, thus confirming the original clinical diagnosis of streptococcal septicæmia. He had in the meantime prepared a *Bacillus coli* vaccine, and the same day gave the patient an injection. From this time recovery was uninterrupted. The patient slept well, continued to feed the child, and got up on November 1st, leaving her room on November 8th.

This is a striking example of the effect of polyvalent serum.

Case 2.—The second case was not successful, but it illustrates the treatment of septicæmia by the use of vaccines, and shows how their use was followed by the disappearance of streptococci from the blood.

The history of the case is shortly as follows: The patient was a young, delicate, and highly nervous woman, æt. 20 years, in her second confinement. Labour commenced on November 7th, and becoming tedious, the child was delivered with forceps the same day. After-pains were troublesome, and suggested to the medical attendant a retained clot, for which he gave warm sanitas intra-uterine douches. The lochia were not offensive. On the 9th the temperature rose to 102° F. There were no rigors, but the patient complained of pain in the right flank. Assistance was called in and the uterus explored on the 10th, a few pieces of doubtful tissue about the size of hazelnuts being removed. That evening the temperature went to 104° F., and early in the morning of the 11th I was called out to see her as she seemed decidedly ill. When I saw her about 3 a.m. she was asleep, but woke soon after. There had been no rigors, nor was any pain complained of. She complained of being faint and giddy. The temperature was 104° F., the pulse about 100. Nothing abnormal was made out on abdominal or vaginal examination. The lochia were sweet, not suppressed, and there was milk in the breasts. She did not strike me as being very ill, but was, however, decidedly neurotic.

It was apparently not a case of sapræmia due to putrid infection of retained clot or placenta. The only question remaining was whether there had been some local infection of uterus with pathogenic organisms. The clearing out of this organ had apparently led to an exacerbation of feverish symptoms, as is not altogether unusual. It was yet early to say what effect the operation would have, and I was not inclined to think she had septicæmia. However, the absence of any very obvious local condition made me cautious as to any very definite conclusion, and I advised a bacteriological examination of the blood and discharge at the earliest opportunity. Dr. Eyre saw her later on the same morning, and the result of his examination was that she was found to be suffering from streptococcal septicæmia. She received in the first instance 20 c.c. of polyvalent serum, but as this produced no improvement in her condition it was followed by treatment with vaccines prepared from the streptococcus isolated from the blood. As the result of this treatment she improved; the temperature fell, and three days after treatment was commenced it ranged between 99° F. and 100° F. It appeared

to us then that we had the disease well in hand, but three days later (the 17th) it again rose to 104° F., oscillating daily between this point and normal. On the 19th I saw her again with Dr. Eyre. At this time the blood showed no evidence of the presence of streptococci, and as she complained of some abdominal pain a local lesion was suspected. I examined her and found some parametritis on the left side. She was now free from septicæmia, and again we had no doubt that the local trouble would subside, and that she would eventually recover. She ran, however, a variable temperature, which from the 26th to 28th appeared to be coming down. I saw her again on the 28th, and was satisfied as to her condition on the whole. She was taking her food well, was sleeping and keeping her strength as well as could be expected. She was then complaining of a little pain about the right side of chest, and there was slight impairment of entry of air-sounds, with a little dulness. She now made a decided turn for the worse, and ran a temperature which remained continuously at 104–105° F., suggesting a recrudescence of the septicæmia. Blood examination, however, showed no evidence of organisms. Exploration of the chest with a needle yielded no signs of pus, but a cultivation of the fluid (mostly blood) withdrawn showed a culture of staphylococci. She died on November 8th, and we find a difficulty in saying exactly why. The signs at the chest became if anything less marked. The parametritis persisted but was not extensive, and there was no obvious pus collection. No post-mortem was allowed. Although this case proved eventually fatal, possibly as the result of some staphylococcal infection of the lung, it is distinctly encouraging from one point of view. The improvement in the first instance from the vaccine treatment was marked, the septicæmia being cured, as was shown by the subsequent absence of organisms from the blood. The local infection of the pelvic cellular tissues and the secondary infection of the lung were, however, more than her system—at the best a by no means strong one—could stand.

I think I have said nearly enough in the account of these two cases to indicate the general line of treatment that I recommend. In one the clinical symptoms pointed strongly to septicæmia, in the other I was doubtful as to its presence. The advantage of a bacteriological examination was obvious in both—in the one as confirming the diagnosis of streptococcal general infection, and the discovery, moreover, of a second infection by *Bacillus coli*, in the second case by actually making the diagnosis. I believe that wherever possible a bacteriological examination should be made in cases of puerperal fever, even when they appear to be slight. For not only do we make the diagnosis certain by doing so, but we obtain the means of preparing the vaccines for treating them. I have already mentioned that in the majority of severe cases of infection, both local and general, the streptococcus is found. On these grounds it is always advisable to treat by giving a polyvalent serum, 20 c.c. to commence with. The marked effect of this is shown in the first case I have described to-day. To sum up shortly:

Sapræmia is not to be regarded as a definite disease; it is the constitutional indication of some local infection, whether by pathogenic or putrefactive organisms. The most important measure to begin with is to determine as far as possible the presence and nature of the local lesion; whether in uterus or vagina; whether putrid clot or infection of wall of genital tract; and to find out as soon as possible the organism or organisms present.

Without bacteriological examination of the blood it is difficult to say whether the lesion is local or whether infection has become generalised.

Owing to the overwhelming importance of the streptococci in puerperal fever it is wise to commence treatment by giving a dose of serum. This, at all events, tides over the twenty-four hours or so requisite for the production of vaccines, and may, indeed, be all the treatment needed. At the same time the preparation of a suitable vaccine should be pushed on with, so that if improvement fails to follow the injection of the serum no time has been lost, and the injection of the vaccine may be proceeded with at once.

September 6th, 1909.

Jaundice in the New-born.—Hasse's reports on the anatomy and physiology of fœtuses and newborn infants demonstrate that the jaundice is the result of the action of the diaphragm causing stasis in the biliary passages. Conditions right themselves as the at first disproportionately large liver becomes reduced in size under the influence of the regular respiration.—*Journ. A. M. A.*, vol. liii, No. 6.

SOME DISORDERS OF THE CEREBRAL CIRCULATION AND THEIR CLINICAL MANIFESTATIONS.*

By ALFRED E. RUSSELL, M.D., F.R.C.P.,
Physician to Out-patients, St. Thomas's Hospital.

LECTURE I.

(*Concluded from page* 328.)

So far we have considered the ordinary fainting fit. We have seen that definite subjective sensations or auræ may attend its onset, that it is often associated with vaso-motor instability, that it may be very sudden in onset instead of gradual, and finally that it may change in type and become epileptic in character. In other groups of cases we have seen marked cardiac and vascular instability with the development of a series of symptoms depending directly on these cardiac and vaso-motor changes. Many of these symptoms are identical with epileptic auræ though more prolonged. We have seen that consciousness may be preserved though modified, that it may almost vanish, and finally that unconsciousness may develop. In all these cases the pathological variations in the circulation are such as to fully account for the unconsciousness and for the epileptic character of some of them.

The phenomena attending a sudden transient and demonstrable arrest of the heart should afford valuable evidence as regards the influence of sudden cerebral anæmia in the production of symptoms. These phenomena can be studied in cases of heart-block.

Cessation of the Cerebral Circulation.

I. *Sudden and Transient.*

(*a*) *Heart block.*—Alfred Webster† records a case accompanied by a series of sixty beautiful sphygmographic tracings which establish beyond question the fact that arrest of the heart preceded the epileptiform attack.

"From the sphygmographic tracings it was seen that there were long intervals during which no pulse was appreciable at the wrist. These intervals sometimes lasted for ten or fifteen seconds. If the finger were kept on the pulse the following facts were observed and noted in order of their appearance: First the pulse became suspended, then, and almost at the same moment, the face became rapidly and extremely pale. If the period of absence of the radial pulse were only of short duration, say of four or five seconds, there was a general *crescendo* return of the pulse and a coincident flushing of the face. During these short pauses the patient appeared to be merely sleeping. Frequently, however, the period lasted much longer, ten, fifteen, and twenty seconds elapsing between the pulse beats. During this time, commencing with the disappearance of the pulse, the pallor of the face became more and more marked. Later on, however (perhaps after some fifteen seconds of absence of pulse), spasmodic twitchings of the face were observed; then as the period lengthened the spasmodic movements extended to the muscles of the neck, frequently carrying the head to one or other side, and ultimately the arms and legs took part in the convulsive movement. Flushing of the face and the return to consciousness were always almost simultaneous with the appearance of the pulse at the radial artery, the pulse being felt slightly before the flushing of the face was observed. Auscultation over the præcordium during these pauses discovered what appeared to be abortive beats of the heart, but these beats were not appreciable to the finger at the radial pulse, or indeed in any of the superficial arteries."

Dr. George Murray,* in his Bradshaw Lecture on "Exophthalmic Goitre," describes the case of a young woman, æt. 22 years, whom he was treating with the preparation of dried milk of thyroidectomised goats, known as "rodagen." Whether the result of the rodagen or not, she developed sudden cardiac failure with bradycardia, and one day "between 7.20 and 11 a.m. she had numerous attacks, in each of which the heart, which was, as already described, beating slowly, would stop altogether for several seconds; a convulsion then took place, which lasted two or three seconds. The patient was conscious at the onset of the convulsion, but lost consciousness for a second or two at the end of it. One or two of these attacks occurred while I was auscultating the heart, and

* The 'Goulstonian Lectures,' delivered before the Royal College of Physicians.

† "Cardiac Arrhythmia in Relation to Cerebral Anæmia and Epileptiform Crises," 'Glasgow Hosp. Rep.,' 1901, vol. iii, p. 413.

* 'Brit. Med. Journ.,' 1905, vol. ii, p. 1379.

the long period of asystole was remarkable; the slow pulse was irregular at the time. After 11 a.m. she had no return of the attacks."

A very good example is recorded by Hay and Moore,* in which the convulsive movements "varied from slight twitching movements and rigidity to a *severe general convulsion*." In their case the periods of ventricular asystole were at times as long as seventy-five seconds. The convulsive movements always came on towards the end of the seizure.

Another most instructive case was recorded by Finny.†

The patient was a woman, æt. 42 years, who suffered from bradycardia and arrhythmia of the heart from April, 1904, to March, 1906. Without entering into any details as to the cardiac condition, it may be stated that the pulse-rate was, as a rule, between 21 and 28 per minute. At varying intervals, however, the rate changed, and a state of pulselessness lasting from five to fifteen seconds supervened. During these latter periods certain fits, or, as she described them, "weak turns," developed. Frequent observations determined the fact that the fits were not simply due to the infrequency of the pulse, for they did not occur while the pulse-rate was as slow as 18 or 20 per minute, but that they were sure to occur when pauses of eight to ten or fifteen seconds were observed, and that they occurred towards the end of the period of cardiac asystole. Dr. Finny gives the following description of the fits:

"A 'weak turn' was ushered in and preceded by a delay in the heart's beat and radial pulse. Thus when a pause lasted seven to ten seconds the patient's face became pale, the eyes had a very pained and frightened look, and some little restlessness of the head and hands ensued, and it ended by a slight flushing of the cheeks, some tears in the eyes, and the patient would give a slight sigh, or little hem or cough, and the weakness would be over. The 'slight fit' came on with a soreness or sharp feeling in the stomach and left side of the thorax, which would then extend up the right side of the chest into the head and eyes. The pallor of the face would be more marked, the eyes would turn up to the right side, and the hands would fidget and the fingers catch at the sheets. The patient always came out of this fit in a more frightened and slightly dazed manner, and the eyes had a strained and somewhat blind look for some minutes. The 'severe fit' was more distinctly epileptic with sudden onset, the patient falling back if sitting up in bed, great pallor, convulsive movements of hands and arms, and also slightly so of feet, unconsciousness for five or ten seconds, and then great flushing of the face, and the patient came out of it very confused, and she was dull and nervous the whole day following. She never bit her tongue or passed urine in them."

Many other cases could be quoted, but the above are enough to justify the statement that cessation of the heart for a limited number of seconds is associated with transient loss of consciousness which may be absolutely indistinguishable from *petit mal* (indeed, Finny regarded and treated his patient for such on first seeing the case), and that with more prolonged cardiac arrest definite convulsive seizures are brought about, which may be practically indistinguishable from those of major epilepsy.

In such cases of heart-block, moreover, the cardiac arrest is the result of heart disease. That the unconsciousness and convulsions in these cases are directly dependent upon a primary failure of the cardiac contraction, and therefore of the cerebral circulation, is obvious.

If evidence is forthcoming that in idiopathic epilepsy a comparable failure of the cerebral circulation occurs, the evidence will be strong that, as in the cases above recorded, the relation between the circulatory failure and the fits will be one of cause and effect. Such a sudden failure in the cerebral circulation might be due to a sudden cardiac inhibition or to a sudden vaso-motor spasm in the cerebral arteries. We will consider both possibilities.

Evidence of Cardiac Arrest in Idiopathic Epilepsy.

Moxon* records three cases in which an epileptiform attack followed an arrest of the heart's action. In only one case was the patient an epileptic, but they are of such value that I will quote them all.

* "Stokes-Adams' Disease and Cardiac Arrhythmia," 'Lancet,' 1906, vol. ii, p. 1271.

† "Bradycardia with Arrhythmia and Epileptiform Seizures," 'Brit. Med. Journ.,' 1906, vol. i, p. 1112.

* "On the Influence of the Circulation on the Nervous System," 'Lancet,' 1881, vol. i, p. 648.

In the first he was examining a patient with cardiac dropsy:

"I was feeling his pulse carefully; the beats were regular and of moderate strength. . . . I missed one, then another beat, and then found the pulse to have stopped so entirely that it made me look up suddenly at the man to see what was the matter. His face had become very pale, his head was turned towards his left shoulder, and the lip and cheek were twitching; the spasms then affected his arms, and he passed into a severe epileptic convulsion. At the time when I first noticed the pulse to disappear the man's arm was quite still. I tried to feel the pulse during the convulsion, but there was so much muscular movement that I could not distinguish it."

On another occasion Moxon was examining the pulse of a man who had been admitted to hospital for uræmic vomiting and convulsions:

"I took his wrist and felt his pulse; it was forcible and regular. I was feeling it when it disappeared from under my finger, many beats being missed. I looked at him; he had become very pale in the face, twitching set in, and he at once went into a very severe epileptic convulsion."

Moxon's house-physician, Mr. Lane, corroborated the same fact twice on the same patient.

Moxon noted a third example in an epileptic:

"I was examining the heart of a young gentleman who was asking my advice on account of attacks of epilepsy. He was standing and I had my stethoscope over his heart and was attending to the quality of the sounds. These sounds stopped suddenly and so completely that in great surprise I moved to look at him, and saw him with exceedingly pale face, evidently quite unconscious, his balance just lost and he falling forwards. He forthwith went into severe epileptiform convulsions."

At the conclusion of his lecture Dr. Southey informed Moxon that, in the only instance in which he had his finger on the pulse at the beginning of an epileptic convulsion, he observed the pulse to disappear during the onset of the attack. Moxon further remarks that—"I have found the pulse present again when the clonic spasms have just commenced." He attributed the cessation of the heart to the action of the pneumogastric nerve, but recognised the fact that the cause of this pneumogastric impulse was yet to seek.

Hilton Fagge* records a similar case. He was listening to the heart of an epileptic when it ceased to beat and the man fell back. Presently it recommenced to beat, and then there was a little twitching of his hands.

The writer† has recorded a similar case coming under his own observation, and another communicated to him:

"The patient, C. T.—,was a man, æt. 21 years. He had suffered from epileptic fits all his life. A maternal aunt had also been subject to fits all her life. The patient's fits commenced with an aura, which was referred to by him as an indescribable sensation in his navel. The majority of his fits occurred in bed at night; sometimes in his waking moments. Any emotional excitement was very apt to precipitate a fit. On April 21st he developed a fit in the out-patient room. He uttered a cry and was seen to be rubbing his hands together. His pulse was immediately examined for, but was not palpable. He was just commencing the stage of tonic spasm when the wrist was seized. Dr. E. W. Hedley, who examined the other wrist, also corroborates the absence of the pulse during the tonic phase. It was not easy to determine exactly when the pulse returned, but we feel certain that the pulse did not return until the clonic phase. At first it was feeble, but as the fit subsided it became fuller and stronger."

Dr. W. T. Harris, of Chiswick, has kindly told me of another case which occurred in his practice.

A man came to have a tooth extracted. While applying the forceps the patient's head suddenly fell back and his face turned exceedingly pale. On feeling for his pulse Dr. Harris found it to be absent. Thinking that it was a severe syncopal attack he attempted to give the patient some sal volatile, but clonic convulsions intervened. These were slight and very transient, consciousness being regained almost immediately. Within a few minutes, however, the patient again turned very pale and became unconscious with toxic spasm. Dr. Harris again noted complete absence of the radial pulse, but at the commencement of the

* Fagge and Pye-Smith, 'Text-book of Medicine,' second edition, 1888, p. 793.

† Alfred Russell, "Cessation of the Pulse during the Onset of Epileptic Fits, with Remarks on the Mechanism of Fits," 'Lancet,' 1906, vol. ii, p. 152.

clonic stage a feeble pulse appeared at the wrist, which gradually improved as the fit subsided. On questioning the patient he acknowledged having had two previous epileptic fits.

The peculiar significance of this case lies in the fact that the complete absence of the pulse and the patient's extreme pallor led Dr. Harris to believe that it was a fatal attack of syncope.

It is not contended that complete cardiac arrest occurs in every epileptic convulsion, for it is stated that the pulse may persist throughout a fit, but an extreme feebleness, short of absolute cessation, might be sufficient to initiate a fit. The following case for example, which occurred under the author's own observation, might well be described as a fainting fit but for collateral evidence.

The patient, T. A—, was a youth, æt. 20 years. He came to hospital having had a "fit" the previous day. He had had only one fit previously, twelve months ago. His facies, however, was typically epileptic. He attended hospital for three weeks, and during that time had one more attack. On his last attendance he complained of pain over a subaceous cyst situated over his right mastoid process. His pulse was 74 per minute, but was small and rather feeble. He flinched on examination of the sebaceous cyst, turned very pale, and rolled back in the chair unconscious. His pulse was found to be extremely feeble. There were no spasms whatever and the unconsciousness lasted for about a minute, when he gradually regained his senses. This attack could only be called a faint. In two or three minutes, however, he again turned pale and fell back, but with this difference, that there were several clonic spasms of his face and one spasm in his arms. His pulse was under examination when he rolled back, and it became so feeble during the period of unconsciousness as only to be detected with considerable difficulty. He was stupid for a few minutes and then recovered. After the attack was over his pulse was still very feeble, but on examination with the sphygmomanometer the blood-pressure was found to be 120 mm. of mercury.

Nobody seeing the boy and the second attack could doubt its epileptic nature, and at the same time the alteration in the pulse in both attacks left no room for doubt but that it was the precipitating factor both of the "faint" and of the "fit."

The Causation of Cardiac Inhibition in Epilepsy.

Moxon attributed the cardiac arrest in his cases to a vagus inhibition of the heart.

Dr. F. H. Clarke,* in a paper on "Epileptoid Attacks in Tachycardia and Bradycardia," quotes Langendorff's observations on the results of stimulation of the peripheral end of the vagus in rabbits narcotised with chloral: "Electrical stimulation of the peripheral end of the vagus causes a prolonged stoppage of the heart, with a very remarkable phenomenon, never hitherto observed, so far as we know,—a complete epileptic convulsion occurs ten or fifteen seconds after the diastolic pause. . . . Precisely similar convulsions are produced by compression of the thoracic aorta at a point nearer the heart than where the great vessels are given off to the head."

Francis Hare† also attributes the epileptic fit to a cerebral anæmia, the result of vagus inhibition of the heart, and assumes further that the inhibition is a reflex act secondary to a widespread vaso-constriction.

There is no doubt that *in epilepsy the vaso-motor system is unstable.* I have been repeatedly struck by the pulse irregularities in epileptic patients. In some the pulse-rate is, as a rule, very considerably increased, and yet on other less frequent occasions it is abnormally slow. Not only that, but the pulse frequently shows wide variations in the course of a few minutes. In two patients I have seen time after time the pulse so feeble and small that they might, on the evidence of the pulse alone, have been in a state of severe collapse. The volume and pressure also vary very considerably. These variations are just as well marked in old cases inured to hospital as in new ones, in whom the pulse might be affected directly as the result of their visit to a hospital.

Spratling‡ notes that:

"In 284 cases in which the pulse-beat was noted it was found to run uniformly above the normal in

* F. H. Clarke, "Epileptoid Attacks in Tachycardia and Bradycardia," 'Brit. Med. Journ.,' 1907, vol. ii, p. 308. Quotes Langendorff: "Epileptische Krämpfe bei peripherer Vagus Reisung," 'Centralb. f. med. Wiss.,' 1878, vol. xvi, p. 65.

† Hare, 'The Food Factor in Disease,' 1905, vol. i, pp. 331, 332.

‡ Spratling, 'Epilepsy,' 1904, p. 271.

189—64 per cent. In 20 cases it was below 70; in 74 cases from 70 to 80; in 161 cases from 80 to 100; while in the remaining 29 cases it was 100 or over. It was counted in every instance during the interparoxysmal period, the patient being entirely free from any immediate epileptic influence."

In an examination of thirty-three cases, to determine the blood-pressure as near to the convulsive period as possible and as remote from the same period as possible, Spratling found an apparent decrease in the blood-pressure just before the convulsive period in eleven cases, and an increase in twenty-one at the same period, the latter being somewhat more marked in degree than the former. The rapid rise in blood-pressure postulated by Hare as preceding the vagus inhibition might be very transient, and, unless the blood-pressure were under observation at the moment preceding the onset of the fit, would be most difficult of demonstration and even of observation. The sensation of chilliness which sometimes precedes a fit is presumably to be attributed to cutaneous vaso-constriction. If, however, constriction should occur in other regions—the splanchnic area, for instance, or in a large muscular area—the result would be the same, viz. either a compensating vaso-dilatation elsewhere, or of necessity a rise in the general blood-pressure. If, instead of the heart responding to this rise in blood-pressure by the customary increased force of beat, its vagus mechanism were too sensitive, or its protecting depressor nerve mechanism at fault, the result might be cardiac inhibition with resulting cessation of the heart, or a marked enfeeblement short of actual cessation, followed by unconsciousness, and if of more than the most transient duration would result in the production of convulsions, *i. e.* an epileptic fit.

It is unfortunate that so few observations of these vascular changes in epilepsy are on record. Unless the heart or pulse happens to be under examination at the moment of onset of a fit the opportunity does not occur, the failure of the circulation is very transient, and the muscular spasms render any examination of the heart and pulse a matter of great difficulty.

It is maintained in these lectures that the fundamental factor underlying both the ordinary faint and the epileptic fit is cerebral anæmia. It follows further that the difference between the two is one of degree rather than of kind. We have had some clinical evidence of this in the suddenness of some faints and in the conversion of faints into fits. The difference I hold to be due to the difference in the rate of development of the cerebral anæmia. In the ordinary faint the cerebral circulation slowly diminishes *pari passu* with the falling blood-pressure. In the fit there is a sudden cessation of the circulation. Similarly the circulation slowly improves in the faint; in the fit it probably returns with greater rapidity.

The fainting proclivity is commonly associated with other evidences of cardiac and vaso-motor instability and an exciting cause is usually present. In epilepsy the ordinary evidences of vaso-motor instability are not so obvious and exciting causes are commonly absent, or rather unrecognised. It must suffice for the present to bring forward the above evidence of cardiac inhibition, however scanty, and to examine to what extent it will explain the various manifestations of epilepsy.

The Correlation between the Circulatory Changes Postulated as the Precipitating Factor in the Epileptic Fit and the Various Symptoms of, and the Recovery from, the Attack.

For any theory of the mechanism of the epileptic fit to rest on a sound basis it is necessary that it should offer a reasonable explanation of, or at least not to be inconsistent with, the various manifestations observed in the attacks. It is submitted that the circulatory failure above postulated does offer a more reasonable explanation than any hypothesis yet brought forward.

(1) *The aura.* — Francis Hare maintains that the explanation of the aura is to be sought in the peripheral vaso-constriction which he postulates as preceding the cardiac inhibition.

"The vascular changes, occurring as they do, synchronously with the rise of blood-pressure, offer a reasonable explanation of the epileptic as they do of the migrainous, asthmatic, and other auræ. Some of the vascular changes may be peripheral and constrictive. Fagge* says: 'The patient perhaps experiences a sensation of coldness or weight in the limb, and the part is found on examination to be pale and cold to the touch, and to have its sensibility distinctly blunted.' Others of the vascular changes may be peripheral

* Fagge, 'Text-Book of Medicine,' 1891, vol. i, p. 751.

and dilative. Trousseau* says: 'A local determination of blood may occur in the finger for instance, causing it to swell, reddening the skin, and rendering it successively within a very short time red, and of a more or less deep violet colour. . . . The swelling is real, not apparent, for rings previously easy suddenly become too tight for the fingers.' Or, again, vascular dilatation and vascular constriction may alternate. Trousseau says†: 'The skin may become excessively pale after having been injected for some time.' But many auræ are unassociated with appreciable objective changes in the part whence they seem to arise. Then it is not unnatural to believe that invisible vascular changes similar in character to the visible peripheral vascular changes just described are taking place in the cerebral centres, and are the immediately responsible factors."‡

That a partial cerebral anæmia is capable of giving rise to the phenomena of an epileptic aura has been demonstrated experimentally by Leonard Hill,§ who says: "I myself have twice produced clonic spasms in myself by compression of one carotid. The first effect on applying the compression was a *sensation in the eye on the same side, then there followed a sensory march of formication down the opposite side of the body. This began in the fingers, spread up the arm, then down the leg.* Finally clonic spasms of the hand occurred, accompanied by an intense feeling of vertigo and alarm."

The association of epilepsy with migraine is well known, and in a unique case recorded by Gowers of a girl who was subject to both migraine and epilepsy, the visual aura preceding the migraine was on one occasion followed by an epileptic fit.

It has been pointed out that some of the prolonged symptoms in the more abnormal faints were obviously vaso-motor or cardiac in origin, and yet were they of momentary duration they would be typical epileptic auræ. Or, as Gowers puts it, in discussing one case with attacks of cardiac and respiratory distress: "Symptoms usually momentary, as the aura of epilepsy, become protracted, extended, as it were into a vagal attack."

(2) *Unconsciousness.*—In the absence of an aura (and it is noteworthy that it frequently is absent), the first feature in an epileptic fit is sudden loss of consciousness. So sudden may it be that the patient falls with the utmost violence. Current views on the pathology of epilepsy afford no satisfactory explanation of this. Yet so dramatic a feature should be susceptible of some simple explanation. The loss of consciousness is not caused by the convulsions. It precedes them in point of time, and in tetanus and strychnine poisoning the spasms may be every whit as severe as those of idiopathic epilepsy, but are not attended with unconsciousness. Now one of the most obvious causes, if not almost the only one, of sudden unconsciousness (excluding severe cranial injuries), is a sudden interference with the flow of blood to the brain. And even in the case of cranial injuries Cannon has concluded that the primary unconsciousness is the result of a cerebral anæmia from reflex cardio-vascular changes.*

The phenomena of the epileptic fit are commonly explained as being the result of an intense discharge from the cortical grey matter. On the motor side this discharge leads to severe muscular muscular spasms, to excessive if disordered function.

As regards consciousness this is absolutely and suddenly lost. I cannot understand how this can be caused by a discharge. It seems to me that the very opposite factor, viz. cessation of activity, must be involved. Consciousness is, I think, too commonly regarded as too mysterious to be governed by ordinary physiological processes, but the brain is certainly very tenacious of this attribute, and a symptom so extraordinarily dramatic and serious as sudden unconsciousness demands an explanation. Save for conditions associated with the vascular system such as cerebral embolism, stoppage of the heart, sudden faints, etc., sudden unconsciousness is almost unknown.

But with a *sudden cessation (or extreme enfeeblement) of the whole cerebral circulation* unconsciousness *must* occur. The phenomena of heart-block show that, in proportion as the period of cardiac asystole increases, we have varying degrees of cerebral failure, transient unconsciousness indistinguishable from that of *petit mal*, attacks with very transient spasm, and finally, definite epileptic fits. Inasmuch as it has been shown that in some cases of idiopathic epilepsy cardiac inhibition does occur, and precedes the onset of the fit, it is difficult to avoid the conclusion that the unconsciousness and fit are the direct results of the cardiac inhibition.

It is noteworthy, also, that sudden occlusion of one large cerebral artery by an embolus produces sudden unconsciousness. A complete cessation of the entire cerebral circulation following upon cardiac inhibition would be obviously a still more potent cause.

In the next lecture the discussion of correlation between the circulatory changes and the phenomena of an epileptic fit will be continued, and the symptoms produced by a more prolonged arrest of the cerebral circulation will be described.

September 6th, 1909.

* 'Clin. Medicine,' New Syd. Soc., vol. i, p. 61.

† *Ibid.*

‡ Francis Hare, 'The Food Factor in Disease,' 1905, vol. i, pp. 335, 336.

§ 'The Physiology of the Cerebral Circulation,' p. 142.

* 'Amer. Journ. of Phys.,' 1902, vol. vi, p. 91.

SPA PATIENTS.

By D. W. RINGROSE GORE, M.B.,
Llandrindod Wells.

It has been said that very little definite information is given by the doctors practising at English spas as to the class of case that does best at their particular spa, and the results of their treatment.

I have tabulated in this paper 1000 consecutive cases as seen by me at Llandrindod Wells, omitting only those cases in which no definite diagnosis could be made—those cases of infrequent disease whose presence was an accident.

It is important to recognise that patients prescribe spas for themselves, that patients discover spas originally, that they find out by experience the diseases that a particular spa benefits. Llandrindod is a very good example of this; for over 200 years it has been a spa always frequented by the Welsh people, many of whom used to drive over a hundred miles to take the waters, and sometimes sleep in their travelling carriages owing to want of accommodation. It had a great vogue 150–120 years ago, when there was a large hotel here, which, however, becoming a great gambling centre, was pulled down by an owner converted during a religious revival. As this left very little accommodation for visitors the English contingent gave up coming here, although it continued to have a large Welsh *clientèle*. I had a patient who was the fifth generation who had regularly come here.

Its fame was widespread 160 years ago. A German physician, Linden, who was afflicted with an inveterate form of eczema, came here to seek relief after trying most European spas; he was completely cured at, and wrote an interesting book on, 'Llandrindod, its Spring and Treatment.' The diseases treated then are very much the same as those which come here now; experience had taught, as there was no doctor at Llandrindod until thirty years ago.

Gout has by far the greatest number—160 patients out of 1000; in this number are only included cases which have had true articular gout. Cases of goutiness are classified according to their most pronounced symptom; together they form over 70 per cent. of cases.

Gout has always been the most prominent disease treated here as far as one can judge by patients' recollections and available records, and gout is almost always successfully treated. One finds patients who come here year after year, often twice yearly, and who remain free from gout as long as they come here, yet if they intermit a year they often get a return of the disease; some of these cases are most striking. Very striking also are those cases which have had regular attacks of gout two or three times a year for many years, and which either cease altogether or are greatly reduced by an annual cure here; the same thing happens at other spas, but I write solely on Llandrindod experiences. It is difficult to say the exact proportion of cures or improvement, as a certain proportion one cannot trace, but of the 160 cases above I only know of five that did not benefit by a course of treatment here.

The waters at Llandrindod which are of most benefit in cases of gout are the sodium chloride springs, which are given in conjunction with a sodium chloride and sulphur water, the sodium chloride water taken early, the sulphur in forenoon and afternoon. Some pathologists say that a sodium chloride water should not be given in gout, but this is a pathological theory which is opposed to all experience, and has really no valid foundation, being based on a theory that sodium chloride lessens excretion, while those that practise at a spa such as this know that excretion is stimulated, the urinary flow markedly increased, an increased excretion of fluids and solids taking place.

Patients have found that spa treatment reduces or prevents gout, and have by experience selected those spas that are of most value in this disease. They are all chloride of sodium springs—Harrogate, Llandrindod, Bath, Kissingen, Wiesbaden, Homburg, Carlsbad, amongst others. The *rationale* of treatment is outside the scope of this paper, which is a record of cases; but I may say that I consider, perhaps because I am the originator of the intestinal toxin as opposed to the uric acid theory as to the causation of gout, that the reason cases of gout do so well here is because of the extraordinary improvement that takes place in the digestive processes as the result of a properly regulated course here, and the lessened intestinal bacterial growth as shown by the indol reaction.

Various forms of dyspepsia account for 120 cases; many of these are gouty in origin. Roughly speaking, almost all cases of dyspepsia benefit by a course here, too; the patient is under control and the diet is more easily regulated than when at home. True hyperchloridrosis as a rule does badly at a chloride of sodium spa, but cases of acidity due to gastric fermentation do well.

Ninety-two cases of rheumatoid arthritis comprise the next most frequent group of cases. These cases, as a rule, do well under treatment, often under internal treatment alone, which suggests that some digestive derangement is a cause of this disease. It is the case in what may be termed the rheumatic group of disease; gout, rheumatoid arthritis, and cases of fibrositis all have symptoms of digestive disturbances, all can be aggravated by errors in diet, and yet probably all have a bacterial origin. To these may be added rheumatic fever, which, if caused by a specific microbe, as it is a chill disease, the microbe which is the cause must be one of those which, as in the case of the pneumococcus, are normally present in a body cavity. As the microbe which has been described as the cause of rheumatic fever is also apparently identical with one of the intestinal bacteria, it is probably a normal inhabitant of the intestinal canal, and under the altered circumstances produced by chill may penetrate the circulation. This is the case with several of the bacteria which are normal inhabitants of the body cavities.

Most diseases to which we are subject can be divided in point of origin into those arising from the respiratory and alimentary tracts respectively; as we know that all diseases of the respiratory tract are caused by the growth of bacteria. I think it a fair assumption that diseases of the alimentary tract are also bacterial in origin.

Gout, rheumatoid arthritis, rheumatic fever, and fibrositis are related diseases. The children of gouty parents may develop gout, rheumatic fever, and fibrositis respectively. If you trace the family history of gouty and rheumatic patients one finds groups of families in which almost all the members of a family will have one or other of these diseases. I know families in which one member will have gout, one rheumatoid arthritis, one eczema and asthma, one sciatica. In the same way you may have a family history of respiratory disease; one gets pneumonia, one bronchitis, one nasal catarrh. Families have the tendency to a group of disease; the individual's peculiarity determines the variety.

Although we may have decided opinions as to the origin of rheumatoid arthritis nothing can yet be proved, yet whatever the cause, we find that treatment directed to the end of improving digestion by increasing nutrition with suitable food and exercise in the open air, by an open-air life, by any means that improve the general health, will have marked effect. A case of rheumatoid arthritis should be treated very much on the same lines as a case of tuberculosis; prolonged treatment by some of the internal antiseptics seems to do good. Rheumatoid arthritis is one of the diseases that do well at Llandrindod; for the reason I think that the conditions mentioned above are a necessary result of a course of drinking, digestion and nutrition are improved, the patient leads an open-air life in a bracing locality, and a certain amount of exercise is essential.

Local treatment is in rheumatoid arthritis useful as an auxiliary means of treatment, only you can no more cure rheumatoid arthritis by baths or massage than you can a case of tubercular affection, but by suitable baths and massage the stiffness and contractions of the joints can be relieved and the patient put into a better condition for receiving other treatment. The improvement that takes place in cases of rheumatoid arthritis in Llandrindod I attribute principally to the internal use of the waters.

Cases of debility from various causes amount to seventy-two cases; these are cases that result from various causes—overwork, influenza and debility uncomplicated by any special disease. These patients benefit by the quiet, regular life they lead and the bracing air of Llandrindod. Some also take a mild course of treatment, which usually includes one of the iron waters.

The various forms of neuritis, excluding sciatica, which has a place to itself, form the next largest group of sixty-eight cases. This is a disease that always does well, especially those cases that have a gouty or rheumatic basis; whether due to inflammation of the nerve itself, or a fibrositis of its sheath, the varied internal and external treatments that can be used almost always cure cases of neuritis.

Eczema with sixty-six cases comes next. This is a disease that with appropriate treatment is almost

always cured. It does not always remain cured, but it is usually lessened in severity for a long time, and with successive courses chronic eczema should be much lessened in severity, if not cured. I only know of three cases in which treatment failed. It is important, as showing the internal origin of eczema, that the majority of cases get quite rid of eczema by internal treatment alone by a course of drinking without any local treatment.

There were sixty-two cases of lumbago. These do well, but lumbago requires more energetic local treatment than most cases of fibrositis.

Rheumatism pure and simple produced sixty-one cases, mostly as after-effects of rheumatic fever. These cases require great care, especially if the attack of rheumatic fever has been recent. I do not think spa treatment is suitable for patients who have recently recovered from rheumatic fever. A warm, sunny, dry climate such as Egypt is by far the best place for them to go to.

Neurasthenia: There were sixty cases of neurasthenia, some simple cases that soon recover with rest and a quiet open-air life, but many belong to that painful class of chronic neurasthenics who drift from spa to spa learned in the merits of their doctors, and faithful in the collection of prescriptions. Many of the women belong to a class of traumatic neurasthenia as the result of operations, usually abdominal. Many women never seem to recover from the mental shock and anxiety that an operation produces, but this is not a factor that is ever considered when the question of operation arises. Surgeons do not see these people in their neurasthenic state; they change their physicians so often that they are not as seriously considered as they should be.

A very interesting and instructive article by Mr. Clinton Dent appeared in the CLINICAL JOURNAL last year, in which he gives many instances of neurasthenia supervening in policemen, often young men, after slight injuries received when apprehending prisoners when, presumably, they are in a state of excitement. These injuries, which may be in any part of the body, may be comparatively trivial, yet, when neurasthenia comes on as a result, it is usually permanent. Any spa physician sees many of these cases of chronic neurasthenia in otherwise healthy women dating from some operation, an operation which had a great effect on their minds, as they regard it as one of the great events of their lives, and are always ready to talk about it.

Sciatica gives rise to fifty-six cases. This is one of the diseases that one can confidently predict will always recover at Llandrindod; there are very few exceptions to this rule. I only know of two. When the full course of treatment is gone through, a curious effect is that sometimes the symptoms do not entirely disappear until a month or so has elapsed after the end of the cure.

Fifty-two cases of heart disease. Many cases of heart disease do well, some do badly; some through carelessness do very badly. When there is a tendency to œdema no heart case should go to a saline spa; and there are few that do not contain chlorides, although their physician may not order a course of drinking, patients sometimes have a course on their own. A patient with œdema of the limbs belonging to the poorer class, knowing the great diuretic effect of the Llandrindod waters will sometimes take a course, with disastrous results.

Cases of irritable heart, of dilated ventricle from over-strain, or after being run down, the obesity heart, the dilated heart, and hypertrophied heart of arterial sclerosis are among those heart cases which do well under appropriate treatment.

Llandrindod is becoming rather a favourite place for people to come to after they return from a residence in the tropics. They get braced up, and a course of drinking greatly improves their debilitated digestive organs. They account for thirty-five cases in the 1000.

Liver also accounts for thirty-five cases; these are becoming a more numerous class of patients. The action of saline water, which gives a local gastro-duodenal lavage and after absorption an increased flow of bile also, as shown by the bacterial infection of the upper intestinal tract, has a markedly beneficial action in cases of cholecystitis. In the same way, too, it restores the liver functions which may have been upset by absorption of bacterial toxins from the upper alimentary tract. Cases in which biliary colic is due to inspissated bile are relieved, small gall-stones passed, and in the case of larger stones the patient is, after a course of treatment, placed locally in a much better state for operation should it be necessary.

Cases of portal congestion are also greatly

relieved, both by the aperient action which can be obtained and by the lessened absorption of toxic products from the intestine.

Renal calculus accounts for thirty cases. This is again an increasing class of case, as the markedly diuretic effect of some of the springs is becoming more generally known. These are usually cases that have passed a stone, or that have been operated upon and come once or twice a year for a wash out with the view of removing any small deposits that might form nuclei for larger stones. The diuretic effect of some of the Llandrindod springs is very marked—indeed, quite as great, if not greater, judging from the experience of patients, than any of the Continental spas.

Anæmia accounts for twenty cases. These include cases of chlorosis, or marked anæmia, which derive benefit from the chalybeate spring. Although the iron contents of the spring are small, yet the hæmatogenic effects are very apparent. The fact that this spring also contains a large quantity of lime salts may help to explain its action on the blood.

Colitis: There were twenty-two cases of colitis in the 1000. This is a disease that does very well; strict dieting, with the improved digestion that a course of saline waters give, soon gives relief, as shown by the gradual disappearance of mucus from the stools. I think in these cases great benefit is derived from the combination of one of the chloride of calcium waters with the ordinary saline. A "Plombière bath" has recently been installed for these cases.

Glycosuria accounts for twenty cases, that is, glycosuria as distinguished from true diabetes. These cases, which are usually gouty in origin, always do well. True diabetes, of which there were five cases, have a temporary improvement; the output of sugar is lessened, the toxic products are diminished, the necessary diet is more easily digested and tolerated, and they benefit in general health by the temporary diminution of the toxic effect of sugar upon the tissues.

Phlebitis, another gouty condition, accounts for sixteen cases, and as in all the gouty group show a rapid improvement under treatment.

Laryngeal catarrh of gouty origin accounts for fifteen cases, which do well with general treatment.

Cystitis accounts for nine cases. When due to enlarged prostate or stone in the bladder medical treatment cannot, of course, give any definite relief: but cases of cystitis or pyelitis due to colon or other bacterial infection seem to improve with the increased diuresis a course of treatment produces. but I have not seen enough of these cases to say whether any permanent effect was produced: I should think it very doubtful.

Arterio-sclerosis gives ten cases, that is, arterio-sclerosis coming for treatment as such, and not found as a complication of other diseases. Blood-pressure soon falls under treatment. I have known it drop from 200 mm. to 150 mm. Hg. in a fortnight. This, I think, confirms the theory that this disease is caused by the absorption of intestinal toxins; the pressure certainly falls and the patient is able to lead a more active life.

There were eight cases of asthma. Most cases of asthma do badly here owing to the altitude and pure mountain air. Occasionally one comes across an asthmatic that does better here than in a town: I am an instance myself, but they are rare.

Psoriasis accounts for eight cases. One can usually get a case of psoriasis well. Prolonged immersion in a sulphur bath alters the patches and they become much more amenable to local treatment.

Obesity gives ten cases pure and simple, but it is also a complication of gout and heart cases. We have a reputation at Llandrindod for the treatment of obesity; certainly there is no difficulty in reducing weight with an amenable patient.

These, then, are the principal diseases for which patients come for treatment at Llandrindod. It will be noticed that over 70 per cent. suffer from diseases of the gouty or rheumatic group and of the digestive system, and that all these cases do well and that the majority get permanent benefit. Of course one expects patients from any curable diseases to do well at a spa. They are under control, their diet and exercise can be regulated, and they are away from home and business distractions, so that their physician has a much better chance of relieving them.

September 6th, 1909.

MICROSCOPIC examination of a smear of the pus taken from a case of Ludwig's angina showed streptococci in large number, associated with bacteria closely resembling the colon bacillus, the latter probably accounting for the distinctly fæcal odour of the pus.—*Journ. A. M. A.*, vol. liii, No. 6.

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COLOSTOMY.

By FRED C. WALLIS, B.A., M.B., B.C.Cantab., F.R.C.S.,

Surgeon to Charing Cross Hospital, St. Mark's Hospital, and the Grosvenor Hospital for Women and Children.

THE operation of colostomy is one which should be much more often resorted to than is the custom at present, as a temporary measure in treating various diseases of the large bowel and rectum.

The reason that it is not so much used as it should be is because the general medical public regard the operation as a last resource, and even then not to be in any way strongly urged. In fact the operation is still viewed from the standpoint of the utility of lumbar colotomy, which, truly enough, was of a very doubtful benefit except as a relief in certain cases of intestinal obstruction. Another objection is that patients with a colostomy wound are, as a rule, unable to keep themselves clean, and therefore unable to go about in public except in a state of apprehension as to their condition. But, as will be shown, there is no reason why this apprehension should exist at all. If the simple precautions are taken which will be mentioned in the treatment people with colostomy openings can go about with almost the same comfort as the normal individual.

It is not proposed here to discuss lumbar colotomy, which was only invented in the days of dread of the peritoneum, a period now past and gone. The fact that the operation could be done without opening the peritoneum was its one and only advantage. In every other respect the operation was undesirable and often ineffective except in those cases in which it was undertaken to relieve obstruction caused by a growth in the rectum.

Colostomy as it is done to-day is more frequently performed in the left iliac fossa than in the mid-line,

but there are many occasions when it is better to do the colostomy in the mid-line.

Colostomy is either a permanent measure or only a temporary one. As a permanent measure it is only used when there is some inoperable stricture or growth below the opening. When such is the case it is much better to divide the bowel completely across, and so avoid any chance of fæcal overflow into the lower segment.

The reason why the operation of colostomy as a temporary measure is one which is not yet sufficiently taken advantage of is because the general practitioner has not yet realised the following advantages of the operation:

(1) The operation is a simple and a harmless one.

(2) The bowel can be opened at once.

(3) Irrigation of the lower bowel can when necessary be carried out on the operation table.

(4) Subsequent washings of the bowel can be carried out as often as necessary, and thus a great deal of absorption of septic matter is prevented.

(5) The affected mucous membrane can be treated by local applications with the best chance.

(6) Cataphoresis can be thoroughly done.

(7) Any tendency of the healing tissues to contract can most easily be prevented.

(8) The closure of the colostomy can be carried out with the greatest ease, and a local anæsthesia is all that is required.

Temporary colostomy can be done for the following bowel troubles:

(1) Certain ulcerative conditions of the colon, sigmoid or rectum.

(2) Bad fistulæ, especially those which communicate with the bladder.

(3) Certain cases of growth which may be so situated that the growth may be excised and the two cut ends of the bowel joined up immediately without any fear of infection from the bowel contents.

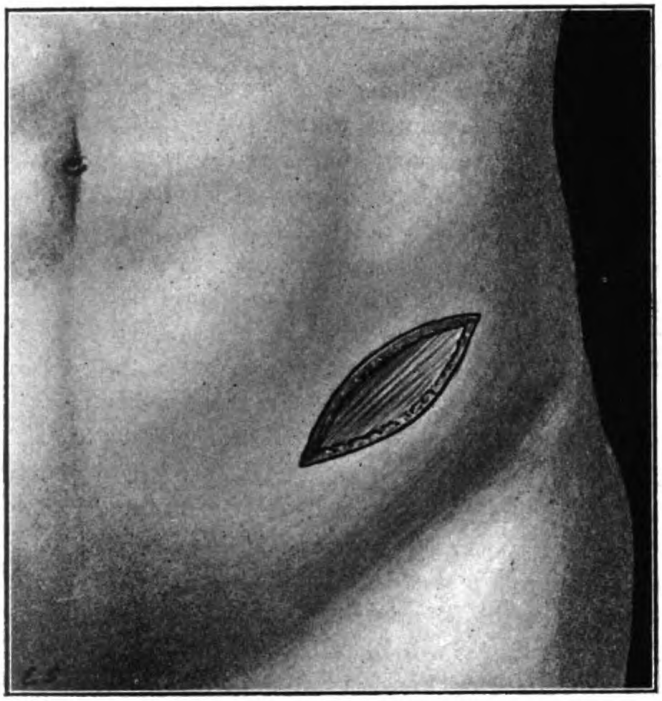

FIG. 1.—Shows the incision down to the muscular tissue.

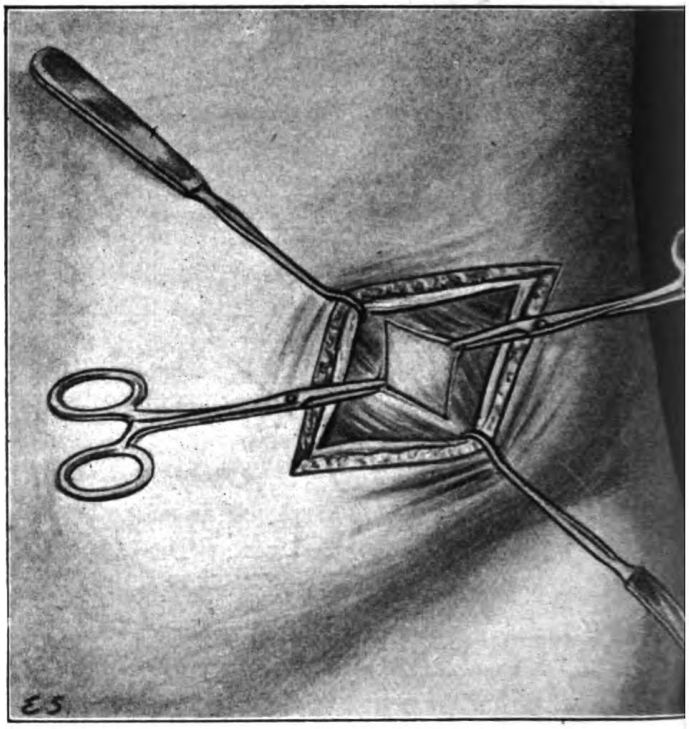

FIG. 2.—The muscle has been split and the deep layer of the aponeurosis is shown.

It is the first of these which is so particularly interesting with regard to this operation.

Non-malignant ulceration of the sigmoid and rectum, whether originating from an infective condition, post-operative or otherwise, or whether it is the after-result of dysentery or due to some streptococcic infection, is rarely cured by any form of expectant treatment, and the tendency of such ulcerations is to get worse. And in those rare cases which do get well of themselves, so to speak, the result is usually one of a bad fibrous stricture, which, as a rule, is the best that can be expected.

As has been said, the tendency of these ulcerations is to get worse. This is due mainly to the fact that the ulceration is carried on by submucous infiltration. If this fact is accepted then it will only be a step further to recognise that any of the ordinary measures are practically useless to prevent the continuance of the ulceration.

A colostomy under such circumstances is the first step towards the proper treatment of certain of these forms of ulceration.

Much has been written and many devices have been made accompanied with alluring diagrams to make a colostomy possess some sphincteric control. One feels sorry to pour cold water on so much inventive talent as has been exhibited in the various operations devised for this purpose; but writing as a practical surgeon, I should say that all such devices are a waste of time and make a simple operation unnecessarily complicated besides greatly increasing the risks of sepsis. However good the immediate results may appear the ultimate condition is that when the so-called sphincter has atrophied a narrow tortuous canal is left through which the bowels are with difficulty emptied, and any attempt to irrigate the bowel is also made difficult, if not impossible, to carry out thoroughly.

The first essential in a colostomy is that the operation shall be performed in such a way that it is impossible for any of the intestinal contents to pass into the bowel below the opening. When the colostomy is permanent this is easily obtained by a complete division of the bowel. But when it is only meant as a temporary arrangement it is necessary that a definite "*spur*" should be made.

Another point of practical importance is that the operation shall permit that the bowel can be opened at the time of operation; this is always a great advantage, and should be made a matter of routine.

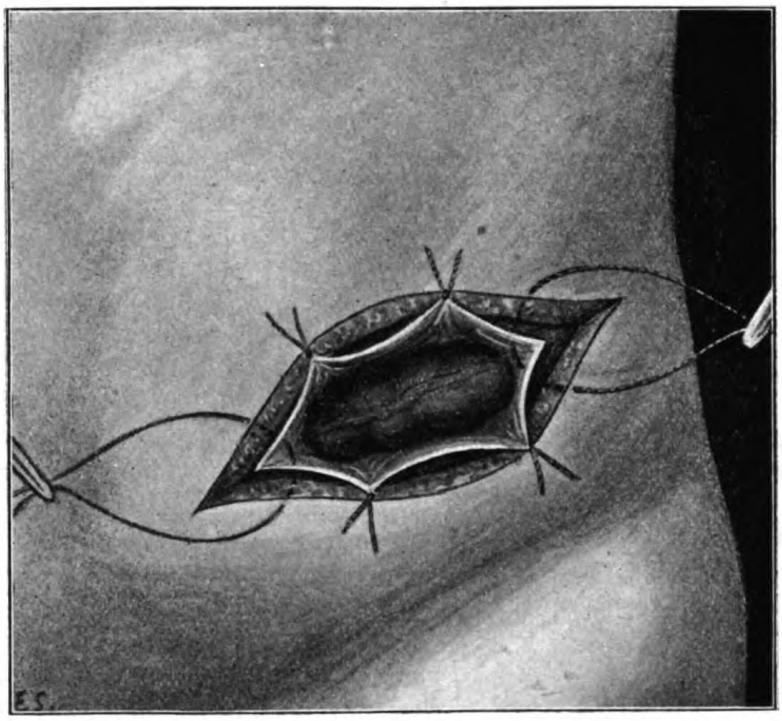

FIG. 3.—Shows the sutures joining the skin to the peritoneum.

I propose to describe the operation which I have been in the habit of performing for the last fourteen years. It is the same as that described in my book on 'Surgery of the Rectum,' from which the diagrams are taken.

Description of operation.—The skin incision $1\frac{1}{2}$ in. long is made at a point about $1\frac{1}{2}$ in. from the anterior superior spine, the middle of the incision corresponding to a line drawn from the anterior superior spine to the umbilicus. The fascia of the external oblique is divided to a similar extent. The muscular tissue of the transversalis is split at right angles to the skin incision and separated until the posterior layer of the aponeu-

rosis is seen; this is picked up with forceps and divided with due precaution to the peritoneum, which lies immediately beneath and which is also opened sufficiently to admit an examining finger. The peritoneum is held apart by forceps, and the finger is inserted into the abdomen and the colon found and pulled up through the incision. At the same time the condition of the colon is made out with regard to any thickening or growth which may exist, and a careful search is then made to establish the course of the colon to avoid opening it in a twisted condition. When these facts have been ascertained a stout silk thread is passed through one of the muscular bands of the colon, which is allowed to drop back into the abdomen. The cut edges of the skin and peritoneum are united with a few fine thread sutures, special care being taken to approximate these two tissues at the upper and lower ends of the wound. Here the thread is passed across from one side to the other and kept long without being tied (*vide* diagram). The bowel is now pulled up by means of the stout silk suture well out of the wound. A needle threaded with stout silk is passed through the skin about one inch from the inner cut edge of the skin and the needle unthreaded. The colon being well lifted up, a pair of shut forceps is pushed through the meso-colon, care being taken to avoid any vessel; after being pushed through, the forceps are opened and grasp the silk suture in the skin, withdrawing the end through the meso-colon and passing it back again through another part of the meso-colon about $\frac{1}{2}$ in. away, and the ligature is tied tightly, thus bringing the included piece of meso-colon close to the skin. It is this detail which produces the spur so necessary for the success of a temporary colotomy.

The bowel is now held up by two pairs of forceps and opened between them. Previous to doing this, however, it should be well packed around to avoid any possible leaking into the peritoneal cavity. The opening of the bowel should be quite small and the cut edges of the mucous membrane are held apart by forceps, any vessel bleeding being clamped at the same time.

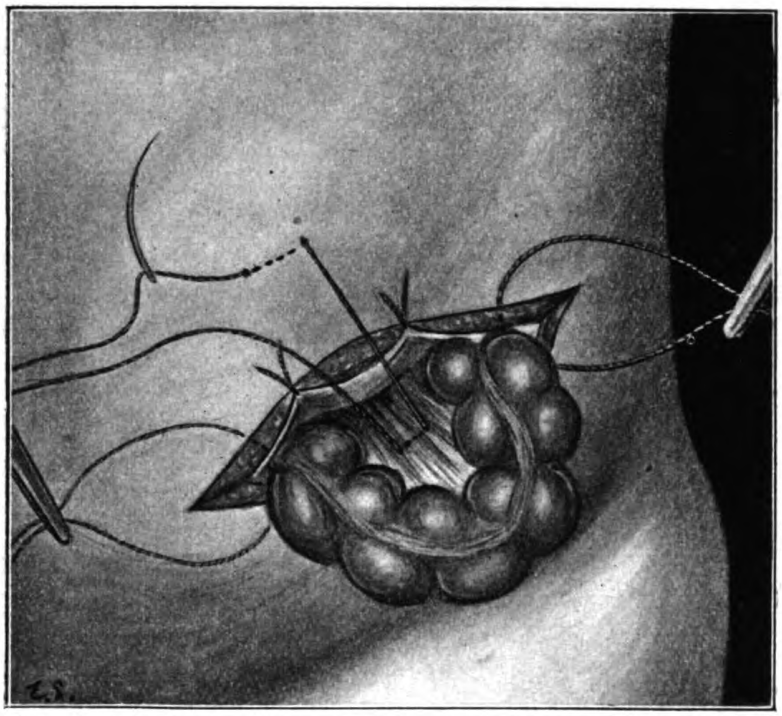

FIG. 4.—The bowel is pulled out and the suture seen passing through the meso-colon and the skin.

A *small* Paul's tube is inserted into the bowel and tied in place by a stout silk ligature which lies in the flange of the tube. All packing is now removed, and the bowel washed over with saline solution. The two sutures at either end of the incision are tied up, and the wound is dressed with an abundance of wool above the gauze to keep the tube in position. A many-tailed bandage keeps the dressing compact and allows the tube to lie

between the folds. The opening of the tube is plugged with a piece of wool.

There is no necessity to apply green protective or any rubber preparation over the exposed bowel; in fact, not only is it not needed, but it is a harmful proceeding.

No fear need be entertained of the bowels acting unduly and there is no need to use any additional rubber tubing on the Paul's tube. The only time when this is necessary is when an over-distended colon has been opened because of obstruction.

Difficulties that may occur during the operation.—The above are the main details in the operation, but there are certain points to emphasise and certain difficulties that may occur which must be mentioned:

(1) All hæmorrhage must be checked before the peritoneum is opened.

(2) There may be some difficulty in finding the sigmoid, especially if the patient's abdomen is either rigid or moving violently, in fact, when the patient is being badly anæsthetised. Under such circumstances if the finger is passed slowly backwards along the parietal peritoneum it must come on to the colon. It may be difficult with rubber gloves to keep hold of the colon, and it is as well to have a sterilised cotton glove to put on over the rubber one whilst manipulating the bowel.

(3) The meso-sigmoid may be quite short, and if in addition to this there is much abdominal fat it may be impossible to bring the colon outside or even up to the skin edge. Under these circumstances the iliac incision must be closed up and the colostomy performed in the mid-line. Median colostomy may be said to be the operation of election in such cases and in most cases where there is much abdominal fat. The reasons for this choice are so obvious that there is no necessity to mention them.

(4) If in tying up the meso-sigmoid a vessel is punctured the hæmorrhage is usually checked by tying up the ligature, but if this does not succeed, care must be taken to stop the bleeding before proceeding further.

(5) If the bowel is either punctured or torn, as may easily happen if the meso-colon is short, it is best to divide the gut completely and tie a Paul's tube in both ends.

(6) Any "appendices epiploicæ" which are present on the exposed colon should be ligatured and cut away.

After-treatment.—An aperient is given on the fourth day, at about which time the Paul's tube will have begun to separate from the bowel; in any case the tube can quite safely be removed by this

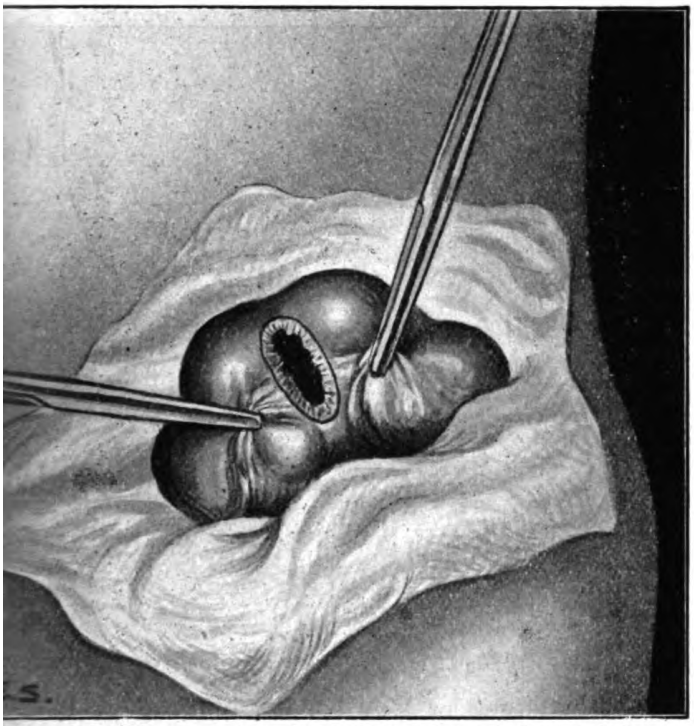

FIG. 5.—The meso-sigmoid suture has been tied up and the bowel opened by a small transverse incision.

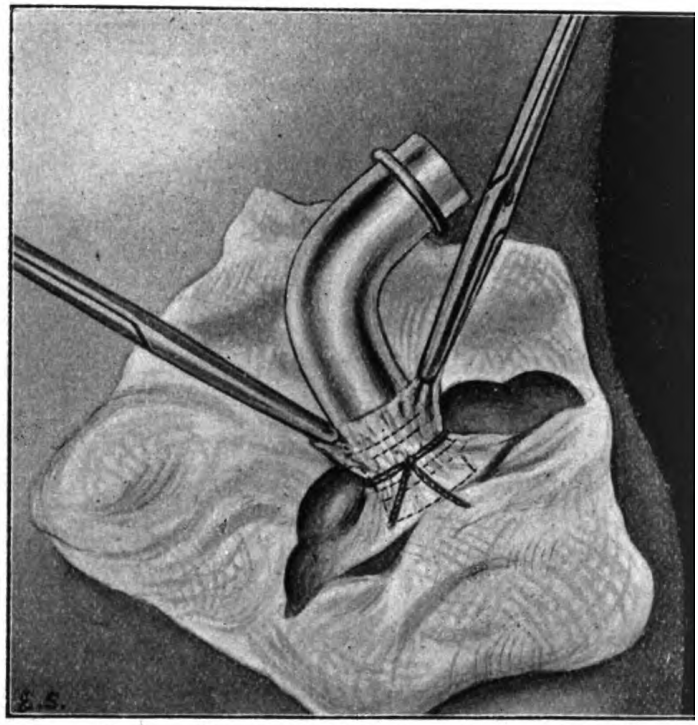

FIG. 6.—The small Paul's tube is tied in position.

time. The suture tying the mesentery and skin together should not be removed until the cæcum has thoroughly emptied itself and the bowel is quiet. If the aperient has not been sufficient it must be followed by an enema. If the suture is removed before this emptying has occurred there is a possibility that the bowel might fall back into the abdomen, owing to straining having caused separation of the newly formed adhesions which occur between the parietal and visceral peritoneum and which help to make the permanent spur.

There is sometimes a considerable amount of œdema present in the exposed bowel, and this is

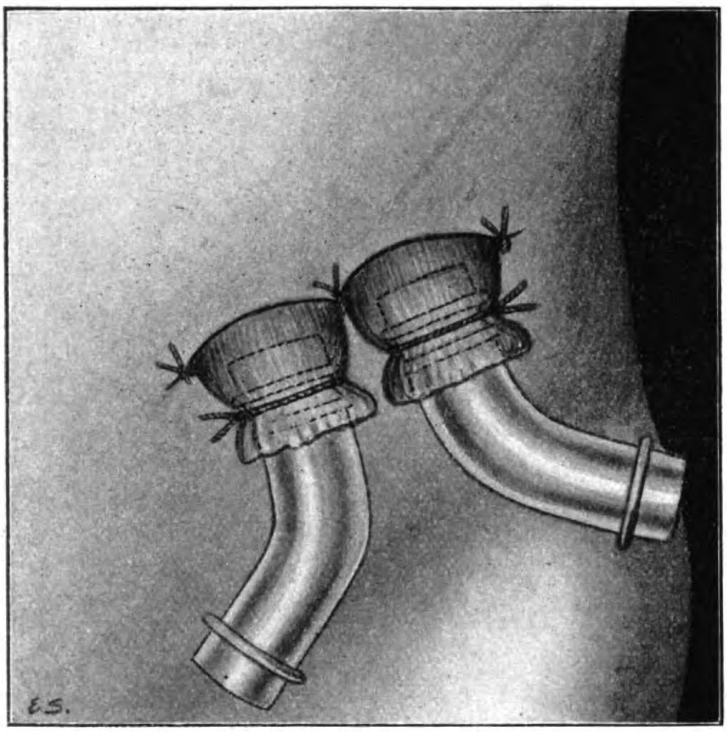

FIG. 7.—Paul's tubes in position when the bowel has been completely divided in a permanent colostomy.

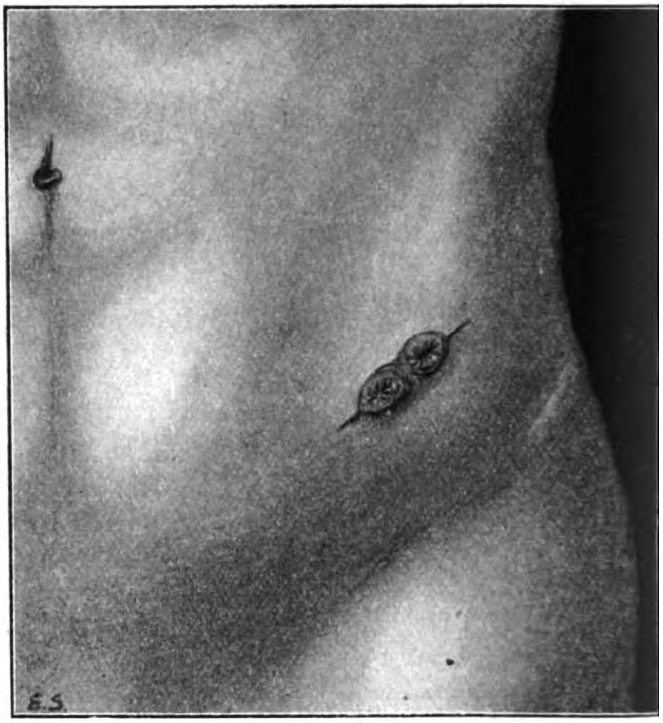

FIG. 8.—Typical appearance of a colostomy two months after operation.

best treated by boracic fomentations for a few days—in fact it may be said that this is a good procedure in *all* cases of colostomy after the bowels have acted; after about forty-eight to sixty hours of fomentation the bowel should be surrounded with dry, plain, sterilised gauze, any stitches which are left being removed. If there is any pus at either end of the wound this is best treated with peroxide of hydrogen. On no account should iodoform be used or an irritating dressing of any sort; it does no good to the wound and too often causes considerable dermatitis.

For thoroughly emptying the large bowel and so enabling the patient to get about in comfort and cleanliness for the rest of the day, the following routine method must be carried out:

For emptying the colon.—A long rectal tube is passed along the upper opening of the colon towards the cæcum, and the outer end is attached to a Higginson's syringe. Between one and two pints of warm water are slowly injected into the bowel, the edges of the colostomy being held together to prevent any backflow from the bowel. This enema is kept in the colon as long as the patient can comfortably bear it (generally about twenty minutes).

The patient is then turned over (face downwards) on to a "slipper" and the water is returned with all the contents of the colon, and firm pressure over the cæcum ensures the complete emptying of the whole of the colon. This should be done with the morning dressing, and the patient is then quite comfortable and clean for the rest of the day.

This simple procedure, if done at a regular time each day, and especially if proper regard is paid to diet, will ensure the patient's comfort provided that there is no intestinal irritation or diarrhœa.

It will be obvious to the practical mind that

this is far more effective and reliable for keeping the patient clean than any complicated operation for the production of a spurious sphincter.

Sequelæ.—Prolapse of the colon may occur from either end of the colostomy, but it is much more common in the upper end than the lower. It does not usually occur until some time after the operation, and then happens in spite of all precautions that may have been taken to prevent it. When it is sufficiently large to become a nuisance it must be dealt with; but in the case of a temporary opening it is better for the patient to put up with the inconvenience for the time being. When, however, the opening is a permanent one, and the bowel has not been completely divided, the colon should be separated from the parietal peritoneum and sufficiently pulled out of the abdomen to overcome the prolapse, and then divided across and the prolapsing portion amputated, leaving enough of the bowel outside the abdomen to enable a Paul's tube to be tied into either end. Both segments of the bowel are kept in place by silkworm-gut sutures, which pass through both sides of the skin including the intermediate meso-colon.

Another sequela which may happen is the reverse of this, viz.: The bowel may gradually recede and the "spur" disappear entirely, thus doing away with all the benefits of the colostomy. Under these circumstances the same method must be adopted as in the case of the prolapse, that is to say, the colon must be separated and pulled out and divided and a Paul's tube tied in each segment.

Should the bowel recede into the abdomen during the first week or ten days owing to want of strength of the adhesions there is no necessity to get panic-stricken about it. A pair of tongue forceps are passed down into the opening and the bowel is gently pulled out on to the surface, and is anchored there by two or three stout silkworm-gut stitches which transfix the bowel and fasten it up to the skin.

Treatment of the lower segment.—The lower segment must first be thoroughly washed through to free it of all intestinal contents. After this has been done, any treatment of the lower bowel can most effectively be carried out without fear of intestinal infection.

When the condition is one of carcinoma, nothing can be done except to keep the bowel as clean as possible by washing through with saline or weak solution of Condy's fluid. Any strong, irritating, chemical solutions should be avoided.

When the lower segment is the seat of dysenteric or other ulceration, healing up to a certain point takes place rapidly, provided that the parts are kept clean. Any ulceration or denuded surface which ceases to heal is best treated with cataphoresis by the method recently described by Dr. Ironside Bruce and myself.

After the healing has taken place, if the pre-existing ulceration has been at all extensive care must be taken that the healed tissues do not contract sufficiently to create a stricture. This can usually be done by the judicious passing of bougies as soon as the contraction commences.

The benefits of this treatment (cataphoresis) in even long-standing cases of infective ulcerative proctitis are well shown in the following case:

Mrs. G—, a married woman, æt 33 years, when first I saw her six years ago was suffering from infective ulcerative proctitis, but refused to have any operation done until the disease had progressed rather far, when an attempt was made to remove the affected mucous membrane. The result of this was a very modified success, and after some months I persuaded her to submit to colostomy. The result of this was in every way satisfactory, and the patient lost all her pain and improved in general health, but the ulceration showed no signs of improvement. About four years after the commencement of the ulceration (*i. e.* two years ago) she was treated with cataphoresis. The result of this was that the ulceration diminished so much that I determined to try and remove the denuded area of bowel and bring healthy bowel to the anal margin. This was done and subsequently the colostomy wound was closed.

Until cataphoresis had been brought to bear on the tissues none of all the various remedies had the slightest effect, but after some weeks of this treatment the result was so marked and the improvement so great that I was not only able to remove the damaged bowel but also to close the colostomy.

Operation for closure of colostomy.—This is an operation of great simplicity, and the results are excellent.

It is obviously useless to try and disinfect the

skin, and the only thing to do is to wash it over with ether on the operation table. The bowel is separated from the skin all round the edge of the colostomy and is pulled out as it is freed until the whole of the width of the colon can be pulled out on to the abdomen. This can usually be done without opening the general peritoneal cavity; but even if this is opened there is no need to be alarmed. The opening in the colon is now sewn up by two rows of continued sutures, and the bowel is washed and replaced into the abdomen, the deeper tissues are brought together by some catgut sutures: *no attempt should be made to bring the edges of the skin together.* The wound is washed over with some strong mixture of peroxide of hydrogen and water and dressed with plain gauze. This dressing is changed every day. No strong purge should be given, but the rectum should be kept empty by enemata and some mild form of aperient should be given on the third day.

Two things are to be avoided:

(1) Too strong a purge.

(2) Overloading of the rectum.

If precautions are taken to avoid these conditions the patient will be quite well in three weeks.

A belt should be worn for some time afterwards, otherwise a small ventral hernia may occur.

The subject matter of this paper has already been published in an American paper, 'The Proctologist,' but I have been asked to publish it in a British paper as well.

September 13th, 1909.

Diagnosis of Incipient Tabes.—Among the points useful for detection of tabes in the early stages is the functioning of the bladder. The patient may regard it as normal when it is beginning to show certain modifications such as delay in micturition after the impulse, relative incontinence at other times, especially after drinking, dribbling of urine during coughing or emotions—all suggesting weakness in the bladder musculature. The patient's denial of venereal infection cannot be relied on, as a rule. Pain suggesting rheumatism, at various points, trigeminal or intercostal neuralgia, is important, as also paræsthesia in the perinæum or scrotum before it develops in fingers, toes or soles.—*Journ. A. M. A.*, vol. liii, No. 6.

SOME DISORDERS OF THE CEREBRAL CIRCULATION AND THEIR CLINICAL MANIFESTATIONS.*

By ALFRED E. RUSSELL, M.D., F.R.C.P.,
Physician to Out-patients, St. Thomas's Hospital.

LECTURE II.

MR. PRESIDENT AND GENTLEMEN,—In the last lecture I dealt first with the ordinary fainting fit, showing how it can merge by insensible degrees into an attack indistinguishable from an epileptic fit. I also dealt with certain prolonged attacks, and I endeavoured to show that the cardiac and vasomotor irregularities, which were the predominant features in the attacks, might fairly be considered as responsible for the varying clinical phenomena and for the epileptic phenomena which were present in some. The influence of arrest of the heart with resultant failure of the cerebral circulation in producing attacks, varying in degree from transient unconsciousness to a severe convulsive fit, as evidenced in cases of heart-block, was adduced. Evidence of cardiac arrest in some cases of epilepsy itself was adduced. Lastly the feasibility of the hypothesis was being tested by an examination as to whether it was capable of explaining, or at least of being consistent with, the various stages of an epileptic fit. I discussed the aura and the unconsciousness. Following these symptoms comes the stage of convulsions. The failure of the heart cuts off the supply of blood not only from the brain but also from the spinal cord and the entire musculature of the body, and the patient falls suddenly.

CONVULSIONS.

The classical experiments of Kussmaul and Tenner prove the intimate relationship existing between a sudden cerebral anæmia and the production of convulsions. Their experiments, moreover, were not masked by the administration of anæsthetics. It is also well known that severe hæmorrhage in man can give rise to a typical convulsive fit. This is not often seen nowadays, but in the old blood-letting times it was common enough, and Marshall Hall† remarks that "convulsion is, after

* The 'Goulstonian Lectures,' delivered before the Royal College of Physicians.

† 'Observations on Blood-letting,' 1836.

syncope, the most familiar of the immediate effects of loss of blood."

(A) *Tonic spasm.*—It is well known that sudden death may occur during exploratory puncture of the chest. In a paper published by the author* on this subject three cases of death occurring during or after this procedure were recorded. In the first the insertion of the needle was immediately followed by sudden death from cardiac failure, and the point of interest in this connection is that it was accompanied by tonic extensor spasm of the arms and convergent squint. The condition of the legs was not observed, but it is very probable that they shared in the spasm. Similarly, as will be shown later, tonic spasm occurred in a case recorded by Cayley in which cardiac inhibition occurred during pleural lavage. It also frequently occurs on experimental ligation of the cerebral arteries in animals. This spasm may depend on the removal of the inhibition influence of the brain, and is possibly allied to the decerebrate rigidity described by Sherrington in animals with transection of fore-brain. It might at first sight be supposed that such spasm should be seen at every death-bed, but in the large majority of cases death is a gradual process, the circulation failing by degrees, the nutrition and irritability of the brain slowly diminishing with the failing circulation, so that any sudden manifestation of spasm would hardly be expected to occur.

In an epileptic fit tonic spasm occurs with great suddenness, and this manifestation is therefore in accordance with what is seen in sudden circulatory failure.

(B) *Clonic spasms.*—In the case of sudden death after exploratory puncture of lung, just mentioned, only tonic spasm was observed. The change from tonic to clonic spasms in an ordinary epileptic fit is of great interest. Long Fox,† who attributed the loss of consciousness and the tonic spasm to cerebral vaso-constriction, ascribed the clonic convulsion to a "gradual yielding of the vaso-motor constriction, allowing at first more blood to enter the arteries than during the period of tonic spasm, but yet far less than is necessary for controlled movement or for rest." They will be referred to again in the next lecture. In this connection a case recorded by Walter Broadbent* is of great importance.

The patient was a lady, æt. 44 years, who had suffered from rheumatic fever in childhood, and showed symptoms of cardiac disease. For seven years she had been subject to epileptic fits. One evening, when talking to her daughter, she suddenly became unable to speak plainly and became rigid. The daughter stated that, instead of the usual fit, there was irregular jerking confined to the right arm and leg; the mouth was drawn over to the right, the head turned to the left. The left arm and leg remained absolutely passive. She passed urine in the fit. She was unconscious for five days after the fit. She then showed complete hemiplegia, hemianæsthesia and hemianalgesia. Movements and sensations were normal on the right side. Death occurred on the ninth day. Post mortem: in the right middle cerebral artery, just beyond the point of origin, a small embolus was found with a distal thrombus for half an inch. The cortex along the course of the vessel was softened; on section the right corpus striatum and all the surrounding parts, including a portion of the frontal lobe, were in a state of extreme softening.

The importance of this case lies in the fact that the patient was the subject of epilepsy. It is presumable that the embolus gave rise to a fit in a subject prone to epilepsy, but the fit was represented by right-sided spasms only. The left side remained absolutely passive, and the embolus in the right middle cerebral artery would prevent the return of blood to the right half of the brain after the cardiac inhibition was passing away.

On the other hand, cerebral embolism is sometimes attended by tonic and clonic spasms of the contra-lateral side, and the absence of such in this case might be urged as evidence against the view that the clonic spasms are due to the return of the circulation. But convulsions are not invariable in embolism, and the obstruction to the circulation need not be complete; an embolus may be arrested at a given point without completely occluding the lumen of the artery. Both the degree of severity of the initial symptoms and the subsequent course

* 'St. Thomas's Hospital Reports,' 1899, vol. xxviii, p. 465.

† 'The Influence of the Sympathetic on Disease,' 1885, p. 252.

* "Cerebral Embolus during an Epileptic Fit," 'Brain,' 1903, vol. xxvi, p. 447.

of the case will depend on this. Loss of consciousness does not always occur in embolism.

In thrombosis unconsciousness and convulsions are much rarer. Owing to the gradual diminution of the lumen of the diseased vessel some degree of collateral circulation may have developed, and the related area of brain has probably adjusted itself to a diminished circulation, and lastly the terminal thrombosis obliterating the vessel may take a very definite time. For these reasons the shock is much less sudden and the nutrition fails rapidly rather than suddenly, and spasm is much less likely to occur. We are, of course, referring solely to the initial spasm of cerebral vascular obstruction, which alone can be compared to the spasm of the epileptic fit. The subject of clonic spasms will be referred to again in the next lecture.

The Physiological Mechanism underlying Recovery from an Epileptic Fit.

Whatever be the immediate factor precipitating an epileptic fit, it is one which is very transient in its action and speedily recovered from. It is one, moreover, which is obviously capable of being brought into action repeatedly. In epilepsy of long duration the patient exhibits a very marked mental degradation, but the effect produced by each fit is imperceptible. Quite apart from the effect produced on the brain by the repeated attacks of cerebral anæmia here postulated as the essential factor of the fit, the intense venous engorgement resulting from the convulsive movements and the asphyxial character of the blood would presumably inflict considerable damage on the brain substance, damage, moreover, repeated over and over again. It would not appear unreasonable to assume that the slight morbid changes described in the brains of epileptics are merely the cumulative results of these lesions. Nothing is more striking than the completeness of recovery from an epileptic fit. Whatever the cause, it seems to pass away absolutely. On the supposition that the fit is due to a sudden transient cerebral anæmia, produced by sudden and transient failure of the cardiac contraction, recovery follows on return of the circulation.

It might be urged that if the fits are due to such cardiac failure it should occasionally happen that the heart should stop permanently, and that death in a fit should be, at any rate, not unknown. If the cardiac arrest is due to vagus inhibition and if this inhibition is sufficiently intense, death might doubtless result, as in the case of sudden death recorded above on exploratory puncture of the lung. But though experimental stimulation of the vagus nerve with a very powerful stimulus does rarely produce permanent arrest of the heart, it is a fundamental physiological fact that there is a practically irresistible tendency for the heart to recommence beating, even during the stimulation—the so-called vagus escape of the heart. We must assume that during arrest of the heart the production of the stimulus material responsible for the initiation of the cardiac contraction, a function centred near the mouth of the superior vena cava, and also the excitability of the cardiac muscle, viz. its power of reaction to the stimulus material, progressively increase until they break through the restraining vagus influence and the cardiac rhythm is restored.

Or it might be that there is a failure of stimulus production with resultant cessation of cardiac activity until, with the accumulation of stimulus material, the heart resumes its beat. Lest this sounds too speculative, I will anticipate what will be mentioned in the next lecture in dealing with status epilepticus, viz. that Mott, in his description of the hearts of people dying of status epilepticus, has described most marked alterations. The heart shows extreme fatty degeneration; the fibres are separated from one another by a serous exudation; they have a lustreless appearance, with indistinctness of striation and accumulation of minute particles of fat in the substance of the fibres. It is greatly to be desired that careful examination of the hearts of people dying of epilepsy should be made by those whose work gives them the opportunity.

This tendency of the heart to recover after arrest is submitted as a feasible explanation of the recovery from major fits.

Post-Epileptic Phenomena.

Though recovery may be very rapid after a mild fit, there is commonly observed after the cessation of the convulsive movements a period during which the patient is comatose, a period frequently followed by natural sleep varying in duration. On the hypothesis of a sudden failure of the cerebral circulation there has been a profound though

temporary disturbance of the nutrition of the whole nervous system. As the result there has been an intense motor disturbance. The sensory side of the brain has doubtless been the seat of an equally severe disturbance, the earliest sign of which is sudden unconsciousness. The initial anæmia of the brain followed by the intense venous engorgement attending the convulsions is enough to account for exhaustion of the sensory elements with resulting coma and sleep. These factors might equally be responsible for the mental disturbance following major attacks.

Those occurring after minor attacks, however, belong to a different category. Mental disturbance is much more common after minor than after major attacks. After major attacks there is commonly a period of coma followed by natural sleep which may restore the equilibrium of the brain. After a minor attack, however, the patient is immediately in full possession of his physical capacity, and any mental disturbance is therefore allowed full play. A very transient circulatory disturbance might well upset those delicate processes which constitute the normal adjustment of the individual to his environment. The exact pathology of such conditions is in the present state of our knowledge impossible of determination whatever view be taken of the pathology of epilepsy.

On Cerebral Intra-vascular Clotting as the Cause of the Epileptic Fit.

According to Dr. John Turner,* "Epilepsy is a disease occurring in persons with a defectively developed nervous system, associated with a morbid condition of the blood, whereby it shows a special tendency to intra-vascular clotting, and that the immediate cause of the fits is sudden stasis of the blood-stream resulting from the blocking of cerebral vessels by these intra-vascular clots." The objections to this view which I raised in a paper on the pathology of epilepsy, read before the Royal Society of Medicine in December, 1907, were: first, that these coagula might be the result of the fit; secondly, that it was difficult to explain the completeness of recovery and absence of paralysis after a fit, if such widespread thrombosis had occurred; and thirdly, that if the clotting were localised it was difficult to realise how it could bring about the extraordinary phenomena of a fit. In a more recent communication* Turner thinks that I have under-estimated the structural defect of the nervous system in epileptics, and that localised thromboses might be efficient in the presence of an easily excitable cortex, and that the absence of gross after-effects are to be explained by the fact that the thromboses occur in minute vessels for which collateral circulation might be readily available. The exact interpretation of the changes observed by Turner is not clear, but in that he attributes the fit to stasis of blood in the cortex we seem to be on common ground, viz. a sudden cerebral anæmia.

Some observations of L. S. Dudgeon† are of interest in this connection: "In the blood obtained from a case of long-standing epilepsy a striking instance of auto-agglutination was observed. The patient's serum, when added to his own red cells, caused a high degree of agglutination. The same effect was observed when the serum was added to normal red cells. In this specimen of blood we have one of the few examples and yet one of the most striking instances of auto-agglutination. In another case of long-standing epilepsy the immune serum failed to react in presence of the immune red cells or normal red cells, but when normal serum was mixed with the immune red cells they collected into large and tight lumps."

I have mentioned this interesting observation in this connection; but it would be, in the present state of our knowledge, a most hazardous speculation to infer from observations on the behaviour of the blood outside the body that similar changes occur within the vessels of the brain.

On Vaso-motor Spasm in the Brain as a Cause of Epilepsy.

This theory of the method of production of cerebral anæmia as the cause of epilepsy has had many adherents. Hallager's monograph upholding

* "The Pathology of Epilepsy," 'Brit. Med. Journ.,' 1906, vol. I, p. 496.

* "Some Further Observations on the Supposed Thrombotic Origin of Epileptic Fits," 'Journ. of Ment. Sci.,' 1908, vol. liv, p. 638.

† "On the Presence of Hæm-agglutinins, Hæm-opsonins and Hæmolysins in the Blood obtained from Infectious and Non-infectious Diseases in Man," 'Roy. Soc. Trans.,' 1908.

this view gives a full historical retrospect.* If, as this paper is written to maintain, epilepsy is due to a sudden failure of the cerebral circulation, then vaso-motor spasm of the cerebral arteries, if intense enough, could certainly act as an adequate excitant of a fit. Direct demonstration of this as the excitant would obviously be very difficult, but if it can be proved that such vaso-motor activity does occur, the possibility of its being concerned in the genesis of some fits would be established. Until recently it was held that there was no evidence of vaso-motor activity in the cerebral vessels, but the demonstration of a copious network of nerve-fibres to the cerebral blood-vessels demands a revision of the position.

Harvey Cushing† notes that, "contrary to the positive statements of many, substances like epinephrin will blanch the pial vessels over the area of its application, as will occasionally a jet of cold water against the brain or the faradic current used for cortical stimulation."

Brodie and Ferrier‡ also found that on injecting adrenalin into the basilar artery of the carefully removed brain, and measurement of the outflow from the torn sinuses, with a moderate amount of adrenalin, distinct diminution of the outflow occurred, and with a larger quantity, complete stoppage.

The phenomena of Raynaud's disease are also worthy of study in this connection. The pathology of this affection is far from clear. In some cases there appears to be no doubt but that the symptoms are due to arterial disease; but it is generally admitted that vaso-constriction in the affected parts is the dominant factor. It is occasionally associated with erythromelalgia. Raynaud§ observed that œdema may precede the attack of local syncope.

Certain ocular and cerebral complications occasionally occur in the course of the attacks of Raynaud's disease which are readily explicable on the supposition of an active constriction of the cerebral arteries.

Thus in Raynaud's new researches* a man, æt. 59 years, with attacks of local asphyxia, also suffered from paroxysmal attacks of impairment of vision. Ophthalmoscopically the arteries were found to be narrowed with here and there partial diminutions, which were actually seen to occur, persist for a certain time, and then disappear under the observer's eyes.

In another case of Raynaud's† a man, æt. 22 years, was subject to attacks of local asphyxia which occurred when the patient went into the open air. The patient also experienced *at the moment of the commencement of the cyanosis a notable obscuration of sight*, which disappeared at the time when the face and hands returned to their normal colour. Opthalmoscopically the retinal arteries were clearly seen to be narrowed when the local asphyxia was at its height, and these vessels *became widened at the moment when reaction set in.*

Raynaud attributed these ocular phenomena to spasmodic contraction of the retinal arteries.

A case of recurrent temporary amblyopia recorded by the late Dr. C. E. Beevor and Mr. R. Marcus Gunn‡ and attributed by them to recurrent spasm of the arteria centralis retinæ is of unusual interest. The patient was a man, æt. 34 years. From the age of seven he had been liable to attacks in which he became suddenly blind for a few minutes, the loss of sight affecting especially the right eye. During these attacks he saw brownish discs and zigzags without colour, and they were not associated with headache. Finally after a severe attack he permanently lost the upper half of the field of vision of the right eye. Subsequently to this he had several attacks, in each of which there was total blindness of the right eye.

"Independently of these attacks he has had at times, ever since he was at school, curious feelings of being tired and dreamy, lasting a few seconds. In these dreamy attacks he dose not lose his senses, but he does not quite remember why he is in a certain place, occurring events do not seem natural, and he has the idea of some impending calamity. They occur sometimes after the attacks of blindness."

On ophthalmoscopic examination in the right eye the optic disc is pale in its lower half and there is evident shrinking of the lower half of the arteria centralis retinæ. The upper vessels and the lower veins look normal. On one occasion a similar attack affected the left eye.

Finally, two months before coming under observa-

* Hallager, 'De la Nature de l'Epilepsie,' 1897.

† Some Experimental and Clinical Observations Concerning States of Increased Intra-cranial Tension," 'Amer. Journ. Med. Sci.,' 1902, vol. cxxiv, p. 400.

‡ Ferrier, 'Harveian Oration,' 1902, "The Heart and Nervous System."

§ Raynaud, "On Local Asphyxia," New Sydenham Society translation, 1888, p. 172.

* Raynaud, *loc. cit.*, p. 155.

† Raynaud, *loc. cit.*, p. 164.

‡ 'Trans. of Ophthal. Soc. of the United Kingdom,' 1899, vol. xix, p. 75.

tion he had an attack "in which he described the symptoms as coldness and numbness in the hands and feet, followed by tonic spasm of the limbs and then by general twitching, but without loss of consciousness." Further, this patient's sister was liable to attacks in which "she has a feeling of contraction, or sometimes sharp pain, at the back of the right eye, and objects appear to recede from her and to get smaller, and finally to disappear in a white fog for a few minutes; the objects then rearrange themselves, and in from ten to fifteen minutes from the commencement of the attack they return to their normal appearance." She was also subject to attacks of ordinary migraine apart from the attacks just described.

Beevor and Gunn also quote a case of Benson's, of Dublin, in which similar recurrent attacks of amblyopia occurred, and in which Benson had the opportunity of examining the fundus during an attack: "The largest division of the inferior temporal artery of the retina was entirely bloodless for about four O.D. diameters of its length, while the other vessels seemed normal. In a few seconds a change occurred, the anæmic portion of the vessels seemed to change its position and moved towards the periphery of the fundus, at times slowly and steadily, and at other times in less regular progression, till it reached the next largest bifurcation, when it suddenly disappeared completely, leaving the whole fundus exactly as he was accustomed to see it."

In the discussion following the paper, Dr. Priestley Smith mentioned a similar case in a lady associated with attacks of ovarian pain and faintness.

The importance of Beevor and Gunn's case can hardly be over-estimated. The neuropathic relationship was shown by the presence of similar attacks and of migraine in the patient's sister.

When we review the symptoms we notice, first, the single attack, in which there was marked vasomotor change in the peripheral vessels as evidenced by coldness, numbness and spasm of the limbs, an attack which may be compared with those described in detail in the last lecture; secondly, recurring attacks of amblyopia, attributed by Beevor and Gunn to spasm of retinal artery. Unfortunately the fundus was not examined in an attack, but in the exactly similar case described by Benson the opportunity presented itself and the spasm was actually seen. Compare also the similar appearances noted by Raynaud in his cases of amblyopia in Raynaud's disease. Lastly there were attacks of dreamy state, so frequently observed in *petit mal*, sometimes occurring after the attacks of blindness. Is any other conclusion open to us other than that the dreamy state was similarly due to arterial spasm in the brain? Such spasm we are of course unable to see, nor do we know the position in the brain which would correspond to the state; but short of actually seeing it the evidence seems conclusive that such must have occurred.

Pal* regards the transitory amaurosis of lead poisoning as being the result of a cerebral vascular crisis.

A most interesting case published by Thomas and Osler† shows the occurrence of epileptic convulsions with attacks of Raynaud's disease.

The sequence of events was as follows:—First, the fingers became cold, white and dead, and the nails blue, associated with considerable pain. Then followed general chilliness, with cold feet. These premonitory symptoms lasted for five minutes, and were succeeded by unconsciousness and convulsions lasting for half an hour. In this case there was, first, the arterial spasm leading to the local syncope of the fingers; and secondly, general chilliness, probably to be attributed to a general cutaneous vaso-constriction.

It seems reasonable to assume that the convulsions were the result of vaso-constriction affecting the cerebral vessels, and it is very interesting to note that Raynaud's disease is apt to be associated with epileptic fits. According to Monro‡ 5 per cent. of the cases of Raynaud's disease have suffered from convulsions at some time or other.

In another case of Raynaud's disease recorded by Osler§ recurrent attacks of hemiplegia and aphasia occurred. The patient was a woman subject to occasional attacks of local asphyxia. In April, 1891, she had her first cerebral attack, comprising dizziness and transient obscuration of consciousness; two similar attacks occurred in the next ten months. During the course of the next four years she had three attacks of aphasia with partial right hemiplegia and one of left-sided weakness. These attacks occurred concurrently with local arterial trouble of fingers and hand. Finally, in January, 1896, there was a severe attack with gangrene of right hand; no aphasia occurred, but she became comatose and died in a couple of days. No post-mortem examination.

The identity of the pathological process underlying the cerebral attacks and the local syncope and gangrene can hardly be called in question. The terminal coma is interesting; the possibility of its being due to cerebral œdema must be considered. The hemiplegic attacks might be due to arterial spasm or œdema, for, as already mentioned, these two phenomena seem to be almost interchangeable in Raynaud's disease.

(*To be concluded.*)

September 13th, 1909.

* Pal, 'Centrabl. f. Inn. Med.,' 1903, vol. xxiv, p. 417.

† "A Case of Raynaud's Disease associated with Convulsions and Hæmoglobinuria," 'Johns Hopkins Hosp. Rep.,' 1891, p. 114.

‡ 'Raynaud's Disease,' 1899, p. 151.

§ "The Cerebral Complications of Raynaud's Disease," 'Amer. Journ. of Med. Sci.,' 1896, vol. cxii, p. 522.

THE PAINFUL SPOTS IN APPENDICITIS.

By M. LEJARS, M.D.,
Professor Agrégé at the Faculty of Medicine of Paris.

As far back as 1889 MacBurney called attention to the painful spot now known under his name in the following terms: "I hold that in every case the seat of maximum pain elicited by pressure with one finger is situated exactly an inch and a half or two inches from the anterior superior iliac spine on an oblique line leading from this point to the umbilicus. This may seem an affected precision, but so far as my experience goes the observation is exact."

Now, although MacBurney's point has become classical, and has acquired an almost pathognomonic significance in the symptomatology of appendicitis, its exact situation has not retained the importance assigned to it by its author, since it is now referred to the middle of a line running from the anterior superior iliac spine to the umbilicus. Then, too, this painful spot has ceased to possess the diagnostic importance which was at first attributed to it. At the present time the actual value of MacBurney's point is a moot point, and is being debated in common with sundry other painful spots of more recent advent with regard to the diagnosis of appendicitis, or as indicating the exact seat of the diseased appendix.

According to Sturmdorf, far from being a pathognomonic sign of appendicitis, "MacBurney's point must be relegated to the modest rank of a possible factor in establishing the diagnosis." We may, however, ask ourselves to what this pain is in reality due. No doubt this contribution to our knowledge is valuable, and the sign in question, if properly sought for, is fixed and durable, as shown by clinical experience. Still, we may well ask ourselves what the pain goes to prove, and we are fain to reply that, taken alone, it proves nothing whatever, since it is wanting in a certain proportion of cases of appendicitis, and is present in other affections of this region, or of some distant region, independently of the existence of appendicitis. We must not say that since there is no MacBurney's point therefore it is not a case of appendicitis; nor ought we to say that because there is MacBurney's point therefore it is appendicitis. Both statements are contradicted by daily experience. Then, too, this MacBurney's point does not in the majority of cases correspond to the appendicitis; it is by no means the result, as we are apt to suppose, of pain simply and solely provoked by pressure on the diseased organ; indeed, the pathogenic explanation is much less simple, and is worth discussing.

There is one well-known fact that must be borne in mind. Appendicitis may exist without MacBurney's point. The pain, it is true, is often situated in the right iliac fossa, but not at this particular spot, being lower down, nearer the pubic arch, yet it is conclusive all the same. Pressure over MacBurney's point sometimes determines pain at some distant point, in the epigastric region or at the unbilicus, for instance, even in the left iliac fossa, under the false ribs, or in the lumbar region, and when this pain is on the left, as shown by Burkhardt, it does not presuppose displacement of the cæcum and its appendix. We must not forget either that in certain cases pressure in the iliac fossa may not determine any pain at all, the painful spot being only detected on vaginal or rectal examination. In confirmation of this symptomatology I may mention two cases: A patient of mine had a huge appendicular abscess, ileo-pelvic; the iliac fossa was distinctly swollen, yet palpation barely caused uneasiness, and there was no distinct localisation. On vaginal examination acute pain was felt on pressure at the bottom of the right *cul-de-sac*, over a very limited area. That was the situation of the displaced, perforated appendix. In the second case a man was brought in with vomiting, high fever and a bad pulse; the pain was originally felt in the right iliac fossa, but there was no tenderness on pressure in that region, the abdominal wall was not distended and could be readily depressed. On rectal examination pressure on the right side gave rise to sharp pain, and on operating it was there that the appendix was discovered.

It would be easy to multiply instances of this kind but it is hardly necessary, and we must admit, with Russell, that these variously distributed, painful spots possess unquestionable value from a diagnostic point of view. It will be seen, therefore, that the absence of tenderness over MacBurney's spot does not justify our discarding the diagnosis of appendicitis. I shall now show

that its presence is not a pathognomonic sign of this affection.

In order to form a correct opinion as to the value of pain in the right iliac fossa we must begin by ascertaining whether the pain is deep or superficial. The superficial pain becomes manifest on the slightest pressure, even mere pinching up of the skin. This is mostly due to propagated pain propagated from some point more or less distant from the spot under examination. Hysterical pain assumes much the same character, and it is complained of, too, in several places. There is not only an appendicular spot but there are median, epigastric, costal and left iliac spots. These are so many "pseudo-MacBurney's spots." Importance must therefore only be attached to pain provoked by a proper method of exploration, *i. e.* by local pressure with the finger-tip.

Even so it may happen under these very conditions that the pain may be due merely to some affection of the abdominal wall. Mathieu relates two instances in which there was sharp pain at MacBurney's spot due to subcutaneous tuberculosis. Moreover, neuralgia of the abdominal wall may cause local tenderness suggestive of appendicitis, and error is especially possible at the febrile period as is shown in the following case reported by Kuttner.

A man, æt. 45 years, just convalescent from a sharp attack of influenza, was seized with an attack of pain in the ileo-cæcal region which kept him in bed five days, when the attack subsided, but there remained some tenderness in the region. A month later a second attack subsided in the same way, only to reappear a fortnight later. Appendicitis was suspected, but although the ileo-cæcal region was tender there was marked sensitiveness of the skin, the wall was easily depressed and deep pressure did not cause any pain. The pain was complained of not only over MacBurney's spot but also at another spot in the middle line, half-way between the umbilicus and the symphysis, another inside and above the inguinal canal parallel with the crural arch, and one over the iliac crest as far as the axillary line. Under these circumstances they diagnosed influenzal neuritis and medical treatment was followed by recovery.

It is conceivable, too, that rheumatism of the abdominal wall—myalgia—may, so far as the pain is concerned, resemble appendicitis. Kuttner records an interesting instance of this in which medical treatment also effected a cure.

Apart from cases of this sort, in which pain at MacBurney's point is consequent upon lesions of the abdominal wall, we must also mention pathological phenomena referable to the abdominal viscera: salpingitis, ovarian cysts, tubal pregnancy, calculi in the ureters, etc. Pain in the iliac fossa may also be secondary to lesions of an organ situated higher up in the abdomen or even in the chest. Gall-stone and cholecystitis must be mentioned in this connection. Grisolle described an "iliac stitch" in pneumonia, and it is by no means rare, especially in children, though sometimes in old people, for this spot to be peculiarly painful and to lead to a diagnosis of appendicitis in the course of early, still unrecognised or ill-defined pneumonia. I have met with instances of the kind myself.

Acute articular rheumatism, indeed, may be mistaken for appendicitis. The following case reported by Kuttner shows this clearly enough. A nurse, æt. 24 years, was seized with severe pain in the ileo-cæcal region along with fever and constipation. In the course of a week her condition got so much worse that an operation appeared to be urgently called for. The temperature was 103° F., the pulse 140, bad, the belly slightly swollen and the abdominal wall very rigid. Peritonitis of appendicular origin was thought of and an operation was performed, but no trace was found of peritonitis, the appendix being free and normal. It was, however, removed, and histological examination subsequently showed it to be free from any trace of recent inflammation. On the following day the abdominal pain had disappeared, and the next day the hand and left foot became painful and swollen and the left leg was œdematous. Acute rheumatic polyarthritis was declared, ran a rapid course and yielded to the usual treatment.

These examples are conclusive, and should always be borne in mind. They show that many maladies may be accompanied by *appendicalgia*, and that, even when well-marked, MacBurney's spot is not *per se* irrefragable evidence of appendicular inflammation.

Now let us inquire what MacBurney's painful spot really does signify. What is the mechanism that causes pain on pressure at this point, and to what deeply seated lesion does it correspond?

It is asserted that the spot in question corresponds to the appendix, that pressure on this spot is transmitted to the appendix, which retorts by a painful sensation when it is diseased. Now in the majority of cases this is not the case.

We must not overlook the fact, to begin with, that the seat of the appendix is far from invariable, that it changes its place just as the cæcum does, and that it is the appendicular cord, the body and tip of the organ, that is met with on this or that surface of the cæcum below or to the inner side thereof, the relationship of which with the abdominal wall it is impossible to specify beforehand. The base of the appendix, that is to say, the area of the cæcal implantation, is more stable, and its intra-abdominal localisation is more constant; it is this appendicular origin of which one has sought to define the relationship with the abdominal wall.

It results from the researches referred to that it is rare for MacBurney's spot to correspond exactly to the base of the appendix, and according to Sonnensburg this point would seem to be opposite the intersection of the bi-spinal line running between the two anterior superior iliac spines and the external margin of the right rectus muscle, that is to say, inside and above the classic pain-spot.

In 1902, indeed, Sir Frederick Treves discussed the very careful anatomical investigation carried out by Mr. Keith on this point: in fifty cadavers the latter found that MacBurney's spot never covered the origin of the appendix, but in reality corresponded with the ileo-cæcal valve. In twenty-two the valve was exactly opposite that spot, or almost so; in fourteen it was discovered above and outside that point, and in fourteen it was below and to the inner side. As a general rule the base of the appendix was met with one inch below the valve, so that here again it was markedly below MacBurney's spot. We may also recall the fact, without laying undue stress thereupon, that Keith, on examining twenty-seven students, found marked tenderness at MacBurney's spot or its immediate neighbourhood in twenty-four.

Lanz' recent researches, moreover, have led him to the conclusion that the origin of the appendix is almost always, if not always, at some distance from the painful spot and obviously somewhat below, and on the strength of this he advises us not to attach overwhelming importance to the classic pain-spot.

Now comes the question: what share must be accorded to appendicular pain in respect of the situation of the diseased organ? Where is the appendix to be found? On which side of the cæcum. Investigating a certain number of cases of appendicitis from this point of view, Dr. Kruger asked himself the following questions: Is the appendix running upwards behind the cæcum? Is it running downwards into the pelvis? Is it to the inner side of the cæcum in contact with the loops of small intestine? Is it in front and to the outer side, underneath the abdominal wall? Unquestionably certain localisations of the pain enable us to state that if the pain on pressure is situated more towards the middle line or a little to the left, if there be an area of pain on the segment of the rectus muscle, the appendix probably runs downwards, lying somewhere near the promontory or behind the bladder, and the concomitant vesical pain, tenesmus, pain radiating down the urethra and felt on defæcation, will confirm this supposition. If movements of the thigh, especially flexion, are painful, we may suspect that the appendix has contracted adhesions with the psoas-iliac muscle.

If, on the other hand, the appendix runs upwards behind the cæcum, in the vicinity of the diaphragm, or over the inner surface of the liver, the diagnosis will be cleared up by finding respiratory disturbances and a subcostal painful spot.

When the appendix is lying free in the main peritoneal cavity the pain is generalised and diffuse, and the vomiting supervenes early and is persistent. According to Kruger early vomiting indicates that the appendix is in contact with the peritoneum of the main cavity, for it ceases as soon as the focus of suppuration is shut off and becomes localised. The same remark applies to abdominal distension.

Speaking generally, the point of maximum tenderness, when clearly defined and fixed, affords a very fair indication of the situation of the appendix, but the area of tenderness spreads as the adhesions become more extensive. Certain is it that without carrying the search for the painful spot too far, thus incurring the risk of setting up hæmatomata of the meso-appendix, of which Dr. Lanz quotes an instance, without departing from an attitude of caution and not neglecting lightness of touch, the direct and indirect exploration of the whole abdominal wall, and especially of the ileo-cæcal region, from the point of view of pain retains its importance in the diagnosis of appendicitis, with the reservation, however, that no exclusive importance be attributed to this or that spot in particular.

September 13th, 1909.

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A CLINICAL LECTURE

ON

THE DIAGNOSIS OF EARLY PREGNANCY.

Delivered at University College Hospital.

By G. F. BLACKER, M.D., F.R.C.P.,
Obstetric Physician to the Hospital.

GENTLEMEN,—I have chosen the early diagnosis of pregnancy as the subject of my lecture to-day because it is a very important matter, and because it is often a difficult problem to decide whether a woman is pregnant or not. From the point of view of practice obviously it is important that you should be able to come to a correct decision, because it is one of those cases in which if you make a mistake in diagnosis your error will certainly find you out. Further, a correct diagnosis of pregnancy may be important from a legal point of view. You may be called upon to say whether a woman is pregnant, because she may have brought an action for blackmail against a man whom she accuses of impregnating her, or you may have to decide whether a woman is pregnant because there is a question of the inheritance of property, and occasionally you may be called upon to say whether a woman who has been sentenced to death is pregnant or not, because as you are aware, one of the reasons for postponing the death sentence on a woman, which the law recognises, is when she is found to be quick with child. A woman, too, may come and consult you saying she is suffering from another pelvic complaint in order that you may carry out some intra-uterine manipulations which will, she hopes, result in procuring abortion. Another legal point arises when a man dies and leaves a widow, who may or may not be pregnant. If she is pregnant the property may pass to her child, or it may go elsewhere out of her

family if she is not pregnant. So that there are a number of circumstances in which a certain diagnosis of pregnancy is of the utmost importance. It is comparatively easy to diagnose pregnancy after the fifth month; the difficulty in coming to a decision arises in the early months of pregnancy. I shall confine my remarks therefore to the earlier months of pregnancy, when you have to rely for your diagnosis upon a physical examination of the patient. In order to render the matter simpler I have written on the board the twelve signs of pregnancy as we usually recognise them. I have placed them in four groups: three symptomatic signs, three developmental signs, three sounds which are heard over the pregnant uterus, and three movements—twelve signs in all.

The symptomatic signs are amenorrhœa, morning vomiting, and the changes in the breasts; the developmental signs are the changes in the uterus, cervix and vagina; the three sounds are the fœtal heart-sounds, the uterine souffle, and the funic souffle; and the three movements are those of the child, the intermittent uterine contractions and the movement of *ballottement*.

I propose to confine my remarks mainly to the period before the fifth month of pregnancy. After the end of the fifth month all these twelve signs may be present; as a rule they are all found to be present if a careful examination is made. If, then, you find ten, eleven, or all of these signs present you may be absolutely certain the woman is pregnant. If you can hear the fœtal heart-sounds, and you are quite sure that the sounds you hear are the fœtal heart-sounds, then you can swear that the woman is pregnant (but you cannot be certain that the fœtus is in the uterine cavity from the fœtal heart-sounds alone). In the early months of pregnancy, say in the first three months, some of these signs are present, but some of them do not appear until the fourth or fifth month.

Let us now consider the changes which occur in the uterus and the signs of pregnancy which are present in that organ in the different months up to the fifth. At the end of the first four weeks there is some enlargement of the uterus, which you may or may not be able to recognise. If you have examined the patient recently and she is easy to examine, that is to say with a thin abdominal wall, and you have made a mental note of the size of the uterus; if she becomes pregnant and you examine her again, possibly, but not certainly, at the end of the first four weeks you may make out that the uterus is enlarged. You may have a suspicion that a woman is pregnant at the end of the first month, but you cannot recognise pregnancy with certainty until the end of the second month as a rule. The uterus, therefore, is a little enlarged at the end of the first four weeks, and the woman has just missed a period. It is four weeks since her last period, and the period which ought to come does not, and this, with the slight enlargement of the uterus, is the only evidence available. It is true that in some women morning sickness occurs within a few days of the occurrence of conception. At the end of eight weeks of pregnancy the uterus measures about 4 by 3 by 2 in., whereas the unimpregnated uterus measures 3 by 2 by 1 in. At this period of pregnancy the uterus is about the size of a goose's egg or a medium-sized orange. It is rather globular in outline, and the main increase in its dimensions is from before backwards. If we consider 3 by 2 by 1 in. as the size of the unimpregnated uterus, you will remember that the uterus at the eighth week measures 4 in. longitudinally, 3 inches transversely, and 2 inches antero-posteriorly; and therefore it is clear that the depth of the uterus is most increased, because the depth is doubled. The main change in the size of the uterus at the end of the second month of pregnancy, therefore, is in the antero-posterior diameter, in which it is very markedly increased. The whole uterus is soft and elastic to the feel, and it presents Hegar's sign of pregnancy. I shall describe more particularly what Hegar's sign is presently, because it is very important. There is in addition some definite softening of the cervix around the external os, the cervix is congested and of a blue red colour, and a purplish tinge of the vulva as a rule can be detected. There is some pigmentation of the areola of the breast, and pigmentation is beginning in the linea alba. These are the chief physical signs at the end of the second month of pregnancy. At the end of the twelfth week of pregnancy the uterus measures about 5 by 4 by 3 in. It is now roughly the size of a fœtal head, it fills up the pelvis, is palpable by the abdomen above the pelvic brim, the cervix is high up and far back, and the normal anteflexion and anteversion of the uterus is increased. At the end of the fourth month or of the sixteenth week the uterus

measures about 6 by 5 by 4 in., definite intermittent uterine contractions can be recognised by the changes they produce in the consistence of the uterus, *ballottement* is present, you can hear the fœtal movements through the abdomen, and you can often feel them on bimanual examination. Quickening usually takes place at about the eighteenth week; it may occur, however, at the end of the sixteenth week, and at this period you may hear the fœtal movements or feel them bimanually. At the end of the sixteenth week the abdomen is beginning to bulge, and the woman is losing her figure. At the end of the twentieth week of pregnancy or the fifth month the uterus measures about 7 by 6 by 5 in., and extends nearly up to the level of the umbilicus, the fœtal heart-sounds can be heard, the patient has quickened or perceived the movements of the fœtus, the secondary areola of the breast is beginning to appear, striæ gravidarum are present in the abdomen, and the parts of the fœtus can be definitely made out on palpation.

Let us return now and consider more particularly some of the physical signs present during the early months of pregnancy. Confining our attention to the first four months, we have to consider the changes in the actual feel of the uterus in the early weeks of pregnancy, because it is in those early weeks that you have to depend on the recognition of the changes in the uterus itself for a correct diagnosis. It is true that the woman may have amenorrhœa, but this may be due to some other cause, and there may be some morning sickness, but that does not justify you in diagnosing pregnancy. Usually there are definite changes in the breasts, but she may be suckling her last child, and if so there will be no signs of any value. In the first sixteen weeks of pregnancy therefore the diagnosis depends mainly on the recognition of definite changes in the uterus itself, and it is these changes which I chiefly wish to refer to. One of the most marked of these changes is extreme compressibility of the lower uterine segment—the so-called Hegar's sign of pregnancy. Marked elasticity of the uterus as a whole is present, and often bulging of one part of the wall of the uterus, together with a difference in the density of the uterus—that is, the part of the uterus occupied by the ovum has a different density from the part not occupied by the ovum, as in the early weeks of pregnancy the uterine cavity is not wholly but only partially occupied by the ovum. Besides this a definite furrow or ridge can often be detected on the uterus, generally on its anterior surface or at the junction of the body and the cervix, and during your examination of the patient, or at different examinations on different days, the consistence of the uterus is found to change—in other words intermittent uterine contractions are present. The anatomical explanation of Hegar's sign is to be seen in the frozen section of a uterus at the tenth week of pregnancy which I show you; the upper part of the cavity of the uterus, as you see, is occupied by the incompressible ovum, while the lower part of the cavity is occupied by the soft, spongy, and very compressible decidua (Fig. 1). Fig. 2 gives you a good idea of the shape of the pregnant uterus at the tenth or twelfth week of pregnancy in many cases. The ovum is supposed to be attached to the anterior wall. You will notice the very marked bulging of the anterior wall of the uterus and the thinness of the lower uterine segment, and further, the degree to which the lower uterine segment can be compressed by the examining fingers is indicated by the dotted lines. If you introduce the examining finger into the anterior vaginal fornix and make pressure on the lower uterine segment, you will find it is so compressible that you can indent it to a considerable degree, and this compressibility will be more easily recognised if you place the other hand through the abdomen on the posterior aspect of the lower segment, and palpate this between the two hands. This compressibility is explained, as I have told you, by the fact that while the upper uterine segment is occupied by the sac of the ovum containing the liquor amnii, the lower segment is occupied by the soft, spongy, compressible decidua. It is filled largely by blood, and by compressing it you can squeeze the blood out of it and compress the anterior and posterior walls together. In some instances the degree of compressibility is so great that it feels as if there were a thin pedicle intervening between the bulging enlarged uterine body and the congested and somewhat enlarged but well-defined cervix. Another physical sign of extra importance, because it is very valuable in diagnosis and is always present, whereas Hegar's sign is only present in some two thirds of the

cases, is the elasticity and ill-defined outline of the uterus as a whole. A student often examines a case of early pregnancy and fails to feel the uterus, not because it is not enlarged but because it is so soft, so elastic, and so ill-defined that he

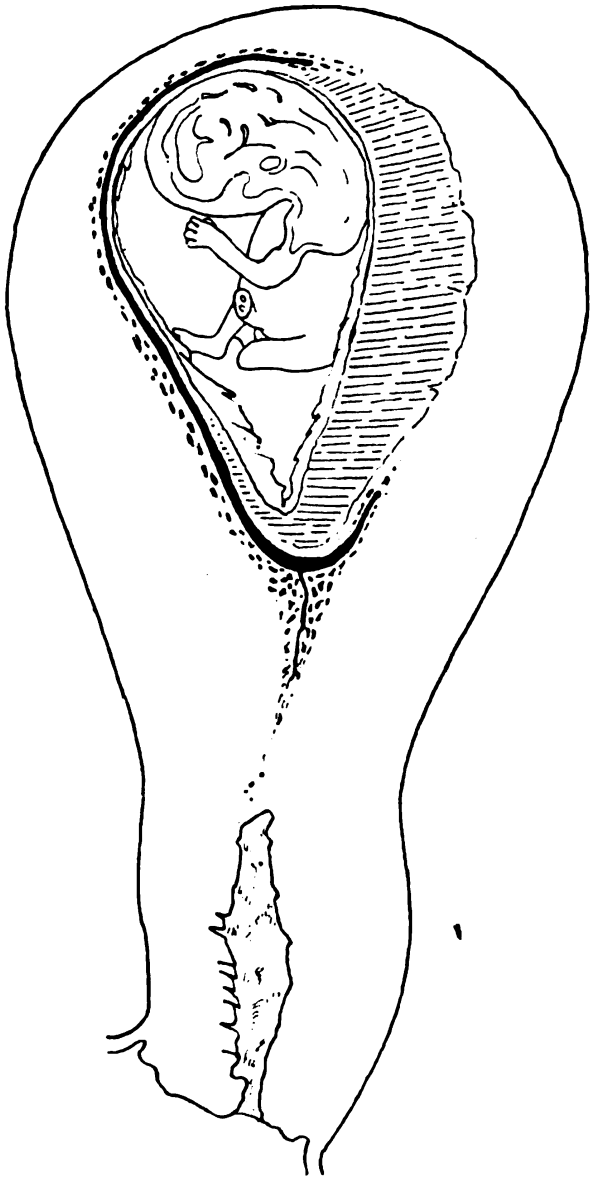

FIG. 1.—Diagram of a frozen section of the pregnant uterus at the tenth week showing the decidual cavity and the lower uterine segment occupied by decidua only.

cannot make out its outline, and he thinks there is nothing there, whereas there is really a pregnant uterus at the tenth week or so. If you feel such a condition of the uterus you may strongly suspect that the woman is pregnant, because it is one of the characteristic signs of early pregnancy. There is another important sign, and that is an irregular bulging of the body of the uterus. The uterus bulges over that area which is occupied by the ovum. This bulging is very characteristic of pregnancy, and often can be felt by the examining finger in the anterior fornix. In some cases the bulging occurs in such a way that looking at the uterus from the front it appears to be developing in an irregular manner. A lateral bulging of the uterus in the region of one of the Fallopian tubes is also a not infrequent condition and is particularly misleading, because constantly it is taken to be something attached to the uterus (Fig. 3). On examining such a case you feel what appears to be the unenlarged body of the uterus, and to the right

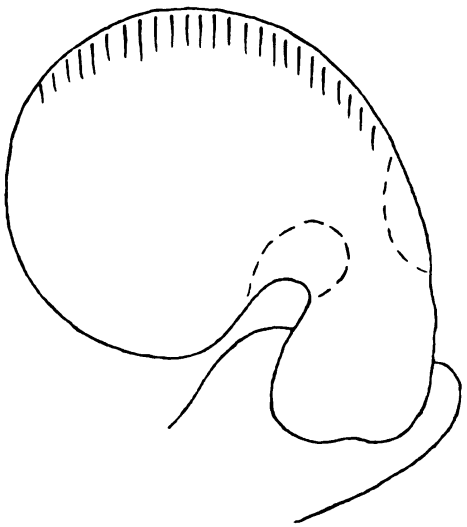

FIG 2.—Diagram of the early pregnant uterus showing marked anteflexion and bulging of the anterior wall of the uterus to which the ovum is attached. The dotted lines indicate the degree of compressibility of the lower uterine segment. After Piskaček.

or left of it you feel a soft elastic body, which you take to be a semi-solid cyst, or a peri-tubal hæmatocele, or a dilated tube attached to the uterus. Further, there is often a very definite furrow, or a ridge between the two parts of the uterus, that occupied by the ovum and that not occupied by the ovum. Such a ridge and furrow may run vertically or obliquely across the uterus, and is very characteristic of an early pregnant uterus, representing as it does the line of demarcation between the developing half of the uterus, the half containing the ovum, and the half which is not developing to the same extent and contains only the decidua. Another important sign is that during your examination, or at subsequent examinations, you find the uterus, which on one occasion felt very soft, elastic

and bulging and very difficult to define, on another occasion feels well defined, hard, and regularly enlarged. This may be of course because there has been an error in diagnosis, but more likely it is because at the time of your second examination the uterus is contracted—in other words an intermittent uterine contraction is present at the second examination and was not present at the first. And the change in consistence of the uterus from one day to another, or during a single examination, is very characteristic

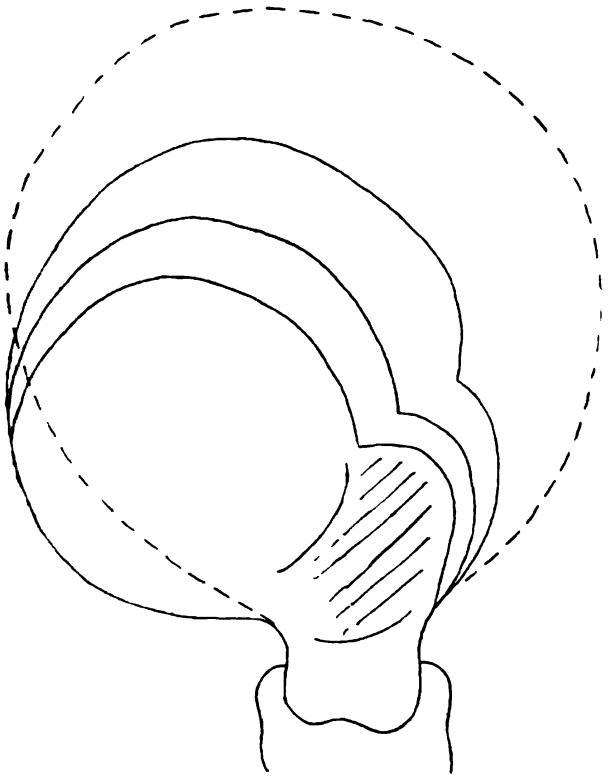

FIG. 3.—Diagram illustrating irregular enlargement of the pregnant uterus in the early months, second, third and fourth, and its disappearance at the fifth month. After Piskaček.

of early pregnancy. To recapitulate the signs, then, in the early weeks of pregnancy you may get well-marked compressibility of the lower uterine segment and elasticity of the whole uterus. You often find an irregular bulging of the uterus at the site of implantation of the growing ovum, and that bulging may be on the anterior wall or on one of the lateral walls, or at one of the tubal angles, because the ovum may be attached on the anterior wall or on the posterior wall, or at the entrance of the Fallopian tube. And it is especially when the bulging is at the tubal angle that it is likely to lead to error in diagnosis. There may be a marked difference in the density of different portions of the uterus—that occupied by the early developing ovum, and that not occupied by it—and you may feel between these two portions a definite furrow and ridge, which separates off one portion from the other. And lastly you may find that the uterus loses any irregularity in outline it may present and becomes well defined and hard owing to the occurrence of an intermittent uterine contraction during your examination of the patient. These are all points of considerable importance in the diagnosis of early pregnancy. Another important physical sign of early pregnancy is softening of the cervix lying round the external os. There are other conditions in which the cervix becomes softened, but such softening usually affects the whole cervix, and does not begin at the external os and spread from thence throughout the remainder of the cervix.

Another point we must now consider is what value has amenorrhœa in the diagnosis of pregnancy in the early months? You may make an examination and conclude that a patient is pregnant some eight to ten weeks, and she may or may not give you a history that she has gone two months over her time. She may say she saw her last period eight weeks ago, and that four weeks ago there was a slight discharge, lasting one or two days. That is fairly common in early pregnancy. You should pay but little attention to the history of a slight discharge at the end of the fourth week. It is not uncommon for such discharge to occur, and it comes probably from the soft decidua in the lower uterine segment, and need not be regarded as of much moment. With such a history you must date the pregnancy back to the last proper period, and not to the partial period, which appeared for a day or two four weeks after the proper discharge was experienced. In other cases, again, you may have to decide whether a woman is pregnant or not who has amenorrhœa, due to the fact that she is suckling her child, and you may have to decide whether the presence of such amenorrhœa is of any value. The occurrence of amenorrhœa when a woman is suckling her child is of course of little value. And in women who are irregular in regard to their menstruation, in whom you get a definite history that they are often two or three weeks over the due date of their period, that the periods come on

only at an interval of six to seven weeks, in such the presence of amenorrhœa is of very little value. Every now and then you are called upon to say whether a woman at or about the age of the menopause is pregnant or not. Such a patient comes to you with the history that she has gone two or three weeks over her time. At this period of life the value of amenorrhœa is not very great; it may be due to the near approach of the menopause, and not due to the occurrence of pregnancy. So amenorrhœa as a sign of pregnancy is only of importance when it occurs in healthy women who have been quite regular up to the time of the cessation of the periods, and in whom the cessation of the periods is sudden, and has not followed a period of irregularity. If, on the other hand, the amount of blood lost at the periods has been diminishing for some time past, the cessation of the periods is not of any particular value.

Next, let us consider the value of morning vomiting as an aid to the recognition of early pregnancy. Morning vomiting usually begins at the end of the first month, at about the fourth to the sixth week, continues during the second and third month, and generally ceases during the fourth month. If the patient has been quite well before, and has no other signs of dyspepsia, and the vomiting occurs in the morning or regularly later in the day, this vomiting is of considerable value. You must of course eliminate morning vomiting due, for instance, to alcohol, and eliminate vomiting due to chronic indigestion, which may complicate pregnancy. In some women vomiting is a very early sign of pregnancy, and they will tell you they are certain that they are pregnant because they have been sick in the morning, although they may not yet have missed a period.

With regard to the mammary changes, they are of special importance in primipara. If a woman is pregnant with her first child, and she has definite pigmentation in the areola of the breast, and especially if she is a blonde and not a brunette, so that the pigmentation is more definite, such a sign is very characteristic. Pigmentation of the areola in multiparæ is not of much value.

During the fifth month of pregnancy the secondary areola, which appears around the primary areola develops, and this is very characteristic of pregnancy.

The changes in the uterus which I have described are of course associated with certain changes in the vagina. These are mainly due to congestion, which produces a slight purple discoloration. On inspection you will find a blue-red colour of the vulva, and of the vaginal portion of the cervix, and this purple discoloration of the vagina is the first sign of pregnancy in that canal which occurs in the early months. Later there is hypertrophy of the vagina and an increase in the amount of leucorrhœal discharge. In doubtful cases of early pregnancy you should pass a speculum, and examine the cervix and vaginal wall to ascertain whether purple discoloration of these parts is present or not.

The uterine souffle may be heard at the ninth or tenth week, but seldom is it heard at that time. It is usually heard first at the fourth month; in the first few months of pregnancy, therefore, the uterine souffle is not of much value. And when you hear it in the early weeks of pregnancy you have to remember that it is generally present with a fibroid tumour, and that occasionally it occurs in connection with ovarian cyst, though very rarely. So it is not of much value, because it occurs in most cases of fibroid enlargement of the uterus as well as in cases of pregnancy. Movements of the fœtus can no doubt occur at a very early period of pregnancy, but they cannot be recognised until the fourteenth to sixteenth week, when they can be felt sometimes bimanually and sometimes by the hand placed on the abdomen. If you can feel the fœtal movements at the end of the fourth month, that is a fact of value. But they cannot generally be felt until the eighteenth or twentieth week, when the woman quickens.

Intermittent uterine contractions I have mentioned, and they can be felt after the sixth or eighth week, not always at one examination, however; but if you make several examinations, you can generally make out some difference in the consistence of the uterus at different times. External *ballottement* can be ascertained about the middle of the fourth month, but even at that period it is very indefinite.

Now with regard to the differential diagnosis of early pregnancy from other conditions, what conditions are you likely to mistake for an early pregnant uterus? Enlargement of the uterus may

be due to small interstitial fibroids, subinvolution of the uterus, old chronic metritis and endometritis, hæmatometra—that is to say, a collection of blood in the interior of the uterus, an ovarian cyst in contact with or close to the uterus, or an hæmatocele. And occasionally an early pregnancy will be diagnosed as present when all that is the matter is a distended bladder. In the diagnosis of early pregnancy you must never omit the safe rule of emptying the bladder and examining the breasts. You will not then mistake a bladder which is full for a uterus which is pregnant. On mere superficial examination these two conditions resemble one another somewhat. But you will greatly facilitate the bimanual examination of the uterus by always emptying the bladder, and you will save yourselves from making mistakes by always looking at the breasts, and this is especially valuable in the case of an unmarried girl. In such a case your suspicion will be aroused by the occurrence of pigmentation. If the areola is pigmented, if Montgomery's tubercles are enlarged, and best of all, if towards the end of the second month, or during the course of the third month, you can squeeze out a little mucoid secretion, you may be very suspicious the patient is pregnant. Therefore follow the rule of emptying the bladder and examining the breasts in all cases of suspected pregnancy.

With regard to the differential diagnosis of these conditions you will find that the diagnosis of early pregnancy from them, apart from the history, which may or may not help you, depends almost entirely on the physical signs—in other words, on the recognition of the characteristic physical changes of early pregnancy in the uterus. And it is for that reason I have laid more stress on the physical changes in the uterus than on anything else. It is true that with a soft fibroid, for example, the patient probably has menorrhagia and not amenorrhœa, but you may occasionally find a patient who is very anæmic with a soft fibroid who has partial amenorrhœa, and if that is so the diagnosis has to be made, not by the history, but by the physical signs. And if you remember the physical signs of early pregnancy and contrast them with the physical signs of a fibroid tumour you will see at once the difference. A fibroid is not compressible in any part of its area; it is not elastic but well defined; it may, however, cause a bulging in the wall of the uterus. A soft fibroid may present differences of consistence between it and the rest of the uterus, and conceivably there might be a furrow or ridge between the fibroid and the remainder of the uterus, but there will not be intermittent uterine contractions. So while differences in consistence and even in the furrows might be present, the characteristic compressibility and elasticity of the early pregnant uterus is lacking in a fibroid. But every now and then it is a difficult matter, and especially is this so if you have a small soft fibroid, and if, further, the patient becomes pregnant. In such a case you may have to wait some little time before being able to come to a definite conclusion.

In a case of subinvolution almost certainly there will be a history that the patient has been confined recently and the outline of the uterus will be that of a uniform, well-defined enlargement; it will not be compressible, it will not be elastic to the touch, and it will not exhibit intermittent uterine contractions. A difficulty that may arise is that a woman with subinvolution of the uterus may become pregnant and then you may have considerable difficulty in diagnosis, because the enlargement of the uterus due to subinvolution will obscure the characteristic physical signs of early pregnancy. Some of the most difficult cases are those in which a woman consults you as to whether she is pregnant or not who to start with has a large, bulky uterus, as in such a case the characteristic signs of early pregnancy may be obscured. And you may have to do what you will have to do often in the diagnosis of early pregnancy—defer making a certain diagnosis until some time has elapsed. In all cases of difficulty and doubt in the diagnosis of this condition, err on the safe side and see the patient again after the lapse of one or two months, because pregnancy is a condition in which the diagnosis is always cleared up by the lapse of time if you only wait long enough. If you wait for a month or two, physical signs which at first are obscure will become clear and can be easily recognised. In chronic metritis and endometritis the physical signs will be the same as in subinvolution. You will find that the uterus is not elastic; its outline is definite and can be readily felt; there are, indeed, none of the characteristic signs of early pregnancy, and there is no amenorrhœa.

The next important thing to diagnose pregnancy from is hæmatometra, because it is associated with

amenorrhœa, and although the amenorrhœa has been present usually some considerable time, yet you may come across a case in which it has been present only a few months, and in which the uterus is definitely enlarged. I have here a specimen of hæmatometra, in which the uterus contains a fair amount of blood, and there is blood not only in the uterus but also in the tube. The patient had had her cervix amputated, and developed complete atresia of the cervix, the menstrual blood accumulating in the interior of the uterus. Such a patient will have amenorrhœa, and the uterus will feel elastic, but it will not be compressible; it will increase in size, but very slowly, and almost certainly you will recognise either atresia of the vagina or of the cervix, or you will obtain a history pointing to some previous inflammation of the vagina or some previous operation on the cervix. So, although theoretically you might confound a case of hæmatometra with an early pregnancy, generally the diagnosis is made with facility. And the condition is one of such extreme rarity that you will seldom meet with a case.

A not uncommon error is to mistake a small ovarian cyst for a pregnant uterus, or to mistake a pregnant uterus for an ovarian cyst. And this is especially likely to occur in a case where Hegar's sign is well marked and some hydramnios is present. You will see from Fig. 2 how a pregnant uterus might be mistaken for ovarian cyst and a non-pregnant uterus. You might imagine the supra-vaginal portion of the cervix represented the uterus, and that the compressible area of the lower uterine segment represented the pedicle, and that its non-compressible elastic body occupied by the growing ovum is the ovarian cyst. This mistake has been made dozens of times, and will be made again. You will not be guilty of such an error if you follow the rule of waiting a month or so in all cases of doubt, or if it is necessary to make a certain diagnosis at once you examine the patient under an anæsthetic. Time will always clear up the doubt, even if under an anæsthetic there is any difficulty in coming to a correct conclusion.

Another important condition from which you have to diagnose early pregnancy is a peri-tubal hæmatocele. This, too, is a not uncommon mistake. A patient consults you with a history of amenorrhœa of two or three months. She has had a little loss, and you think she has had a threatened miscarriage. You examine the uterus, and you find what you imagine is the body of the uterus hard and tense, and another part of the swelling soft and elastic, and therefore you think she has probably an extra-uterine gestation. In the condition represented in Fig. 3 you might imagine that that undeveloped half of the uterus is the uterine body, and that the developed part is a pregnant tube adherent to the uterus, or lying in close contact with it. Such an error is easy, and it is constantly being made, because the patient has some of the signs of pregnancy, namely amenorrhœa, and probably morning sickness, and there may be also hæmorrhagic discharge from the vagina. You may attribute that to a threatened abortion, and you may imagine that the unilateral enlargement of the uterus, which is not uncommonly present in early pregnancy, is a peri-tubal hæmatocele adherent to the uterus, and in that case you will diagnose extra-uterine gestation, whereas the patient has in reality an ordinary intra-uterine gestation developing in one horn of an arcuate uterus, or developing more on one side of a normal uterus than on the other. Here, again, the condition is cleared up by waiting a little while, because in the course of time, by the fourth or fifth month, the uterus regains its normal pyriform shape, the irregular development of one portion of it has disappeared, and with this the resemblance to a peri-tubal hæmatocele. Fig. 3 shows the anatomical basis for such a mistake, and how at the end of the fifth month the uterus has resumed its normal shape, and has become quite easy to recognise as a normal enlarged pregnant uterus.

Those are the common conditions, then, which you are likely to mistake for early pregnancy: soft fibroids, subinvolution of the uterus, enlargement of the uterus due to chronic metritis, hæmatometra, ovarian cysts in proximity to the uterus, and peri-tubal hæmatocele. And I would like further to point out how often a retroverted pregnant uterus is mistaken for a peri-tubal hæmatocele. In such a case you feel a soft swelling in Douglas's pouch which resembles both the elastic pregnant uterus and the soft, doughy feel of an hæmatocele. You may mistake a retroverted gravid uterus for a peri-tubal hæmatocele, or a peri-tubal hæmatocele for a retroverted uterus, and you may make the grave error of trying to replace such a tumour. The diagnosis of this condition is particularly important, because if you attempt to replace a peri-tubal hæmatocle thinking it is a retroverted gravid uterus you may rupture it, cause severe hæmorrhage, and place the patient's life in considerable danger. In all such cases of doubtful early pregnancy, if it is essential to make a diagnosis at once carry out a careful bimanual examination under an anæsthetic, or if there is no urgency about the case, wait, and time will clear up any doubtful points and render the diagnosis quite easy.

Remember the dictum of the celebrated French obstetrician Mauriceau: "If there is any doubt about a case of this kind it is better to wait patiently than to make your prognosis in a hurry."

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SOME DISORDERS OF THE CEREBRAL CIRCULATION AND THEIR CLINICAL MANIFESTATIONS.*

By ALFRED E. RUSSELL, M.D., F.R.C.P.,
Physician to Out-patients, St. Thomas's Hospital.

LECTURE II.

(*Concluded from p.* 365.)

Migraine.

The association of epilepsy with migraine is of considerable interest. It occasionally happens that periodical attacks of migraine are replaced by ordinary epilepsy, the migraine then ceasing. In migraine there is undoubted evidence of abnormal vaso-motor action. Chilliness of the skin is common: the temporal artery on the affected side is often contracted and hard. Relief of the pain often attends compression of the carotid artery. This, and the fact that the pain in the head is of a throbbing character, suggest that the old explanation of the vaso-dilatation of the cerebral vessels is correct. Such a dilatation of the vessels, with resultant increased tension of the dura, etc., would be enough to account for the pain. The brain tissue itself is insensitive, and Harvey Cushing has noted that after excision of the Gasserian ganglion any subsequent headache is only felt on the side with the intact fifth nerve, an observation which indicates that intra-cranial pain is experienced *via* the branches of the fifth nerve to the dura and membranes of the brain. The dilatation can, moreover, be seen. Thus Mollendorff† points out that "during the attacks the background of the eye on the suffering side was of a bright scarlet red, the optic papilla red and œdematous, the arteria and vena centralis retinæ enlarged, the latter knotty and very tortuous." There is much to be said for the view that the symptoms of migraine depend upon abnormal vaso-motor activity, and that the headache is the result of vaso-dilatation.

Gowers‡ records the following cases:

In one, a woman, æt. 38 years, had been subject to migraine from the age of six. For many years when the pain was most intense she suddenly felt a peculiar sensation at the epigastrium, which passed up through the chest to the head, and seemed to spread over the whole head. It continued for ten minutes, and ended as suddenly as it began with an eructation of flatus. During the sensation she was unable to see, or to speak, or to understand what was said to her. She heard words as sounds but could not tell their meaning. When the sensation ended sight returned, and her power of speech came back gradually; at first on trying to say a word she could not utter it correctly. At the age of thirty-three this sudden state became a definite epileptic fit. When the headache reached its height she lost consciousness; general convulsion occurred, with tongue-biting and micturition. These fits became her chief trouble and they always occurred during the course of the headache.

The epigastric sensation, so common an aura in epilepsy, was discussed in the last lecture, and it was suggested that it was due to a sudden splanchnic dilatation. The condition of the patient after it occurred was very similar to some of the cases of so-called vagal or vaso-vagal attacks. The replacement of this state by an epileptic fit may be explained by a more sudden splanchnic dilatation or by a severe cardiac inhibition concurrent with the splanchnic dilatation.

In another the patient was a girl, æt. 16 years, who had been subject to periodical attacks of migraine since the age of five years. At thirteen and a half she had an epileptic fit during sleep, and since then three others—two during sleep and one when awake. Since the first fit the headaches had been frequent, but were preceded by a brief but very definite visual aura. The interesting point is that the single epileptic fit which occurred when she was awake was preceded by precisely the same aura. An interpretation that is possible for this case is that local vaso-constriction was responsible for the premonitory visual manifestation, and was succeeded by a local vaso-dilatation in the attacks of migraine, and either by a more severe and widespread cerebral vaso-constriction or by cardiac inhibition in the epileptic attack.

Migraine is also occasionally accompanied by transient aphasia. Conditions such as these suggest very strongly that abnormal vaso-motor phenomena are concerned and transient spasm

* The 'Goulstonian Lectures,' delivered before the Royal College of Physicians.

† See Liveing, 'Megrim and Sick Headache,' 1873, p. 307.

‡ 'Borderland of Epilepsy,' p. 93.

of cerebral arteries is not an unreasonable hypothesis.

The evidence for the existence of vaso-motor activity in the brain is therefore partly direct and partly indirect. It is obviously a matter of great difficulty in clinical work to demonstrate such alterations, owing firstly to their evanescence, and secondly to the fact that when they have subsided no evidence of their existence is left behind.

Petit Mal.

A consideration of the cerebral phenomena attending cases of heart-block shows us that the attacks present an increasing degree of severity proportional to the length of the period of asystole. There may be merely a transient giddiness, a dazed feeling, a "turn," or the head may drop forward momentarily, the patient recovering himself immediately; or unconsciousness may be rather deeper though still transient; or a fall with slight spasm; or, finally, a severe general convulsion. Every one of these phases could be duplicated among the numerous manifestations of minor and major epilepsy. And when we compare the gradually increasing severity of the manifestations, according to the length of the period of cardiac asystole, with the phenomena of epilepsy, the resemblance is more than suggestive.

Discussing the types and degrees of seizures, Aldren Turner* remarks that—

" . . . The primary types of epileptic attacks denote consecutive stages of the same series of phenomena—stages which may be arrested at any period."

Among various examples given by Turner is the following:

"A common form of incomplete attack is seen in fits, the aura of which is a feeling of giddiness followed by a sudden fall from loss of consciousness, but without convulsion. In these cases there are commonly found attacks of giddiness (aura), as well as complete seizures, in which the fall is followed by the usual convulsive phenomena of a major fit."

In other words, the stages of severity observed are, firstly, an attack of giddiness only; secondly, an attack of giddiness followed by a fall; and, finally, the complete fit, terminating in convulsions.

In a case of my own, a girl, A. L—, æt. 12 years, was subject to both major and minor attacks, the latter being described as attacks of giddiness. She has suffered from epilepsy since the age of six. On one occasion I was feeling her pulse. She was telling me of her state during the past fortnight and was saying that she was that day feeling perfectly well. She was not nervous at the time, but suddenly the pulse stopped; she gave a short cry, clutched at my coat, and sat down in a chair by which she had been standing. She did not lose consciousness. The cardiac arrest was of very short duration, probably about five seconds, and the heart then began to beat again, but the pulse was extremely feeble for a few contractions, perhaps from fifteen to twenty, and then rapidly increased in force so that within about half a minute from its reappearance it had regained its previous state. A few minutes later its rate was 124—a rate very common in this particular case. The above attack was a typical example of many of her minor seizures. She herself complained of giddiness and thought she was going to have a fit, as this sensation usually preceded a major attack, though an accompanying aura, a feeling of a desire to micturate, was absent. The child is always much frightened by these attacks.

Here was a case of cardiac inhibition in what would be called *petit mal*, but which I think would be more accurately described as an incomplete or abortive major attack. The cessation of pulse and the child's cry were, I think, simultaneous. Had the cardiac arrest been of longer duration a fully developed major attack would doubtless have occurred.

Again, in Finny's case of bradycardia recorded in the first lecture, the attacks varied from what were called "weak turns" to "slight fits" and "severe fits." The case was at first regarded as one of *petit mal*. It is very interesting to note that the slight fits came on with soreness or sharp feeling in the stomach and left side of the thorax, which would then extend up to the right side of the chest into the head and eyes—a definite aura in fact.

Here we have an aura, and if it had occurred in a case of idiopathic epilepsy it would have been regarded as typical, but it occurred in a patient whose attacks were unquestionably secondary to cerebral anæmia from heart block. Whether the aura was due to sensations derived from the

* 'Epilepsy,' 1907, p. 69.

peripheral vessels and heart, or to cerebral changes resulting from the cessation of the circulation, it is difficult to say, but there can be no doubt that it was of circulatory origin.

Finally, in the severe fit in the same patient the onset was more sudden; there were convulsive movements of limbs, and the patient came out of it very confused, and was dull and nervous the whole day following.

Such resemblances are too close to be due to mere coincidence. It is difficult to conceive of any other explanation than an identity of cause. The cause was unquestionably sudden failure of the cerebral circulation in the case described, and the conclusion seems inevitable that some attacks of *petit mal* are determined in a similar way.

But it cannot be claimed that cardiac inhibition occurs in all cases of minor epilepsy. Moxon* quotes Hughlings Jackson's observations of the disappearance of the pulse at the onset of attacks of *petit mal*. I myself was on two occasions feeling the pulse of a boy subject to minor attacks when one supervened. No arrest occurred nor was there any obvious change in the pulse-rate. Evidence has been adduced as to the occasional occurrence of transient spasm of the cerebral arteries, and such spasm may underlie these attacks. It is suggested, therefore, that two factors may be concerned in the production of *petit mal*. Some cases may be due to very transient cardiac failure and others to transient spasm of the cerebral arteries.

Infantile Convulsions.

The similarity between infantile convulsions and those of idiopathic epilepsy is so close that the probability of the same factor underlying the two conditions must be very considerable. The vaso-motor system of the child is much more unstable than that of the adult, and the ease with which emotional disturbance and shock are produced is notorious. In a considerable number of cases the occurrence of apparently ordinary infantile convulsions is the starting-point of chronic epilepsy; in other words, of the enormous numbers of children affected with infantile convulsions, some become chronic epileptics while others do not. There is nothing in the type of the fits which enables us to determine whether chronic epilepsy is likely to follow or not.

It seems hardly open to doubt but that the large numbers of alleged causes of infantile convulsions, such as teething, rickets, worms, acute infections, gastro-intestinal disturbance, fright, and so on, must exert their influence *via* some common factor. Such a factor might be, as suggested, abnormal vaso-motor and cardio-motor systems with a ready liability to attacks of acute circulatory failure, either from cardiac inhibition or from splanchnic dilatation. If this factor is brought into play once only we have an isolated convulsion; if only a few times we have a few convulsions. If, however, it is brought into action over and over again, chronic epilepsy is the result.

Children are more susceptible to fear than adults. Discussing the effects of fright, J. R. Charles* remarks that:

"As regards the vaso-motor apparatus, there is widespread vaso-motor constriction of the cutaneous area, with a feeling of chilliness, shivering, and goose-skin. At the same time there is probably a corresponding vaso-dilatation of some of the internal vessels, as evidenced by the copious secretion of urine, and also by diarrhœa. As a rule the heart beats quickly and violently, but if the impression is very sudden and intense there may be *complete arrest of the heart's action*. There is frequently a spasm of some of the involuntary muscles, leading to involuntary micturition and less frequently defæcation, and a feeling of oppression and constriction in the chest, possibly due to contraction of the bronchial muscles. . . . Tremor is so common that the verb 'to tremble has become almost synonymous with the verb 'to fear.' . . . More rarely the muscles may become rigid, or be *thrown into convulsive movements during moments of great terror*. . . . It will be noticed that there are certain points of analogy between the bodily effects of fright and those of cold, viz. the cold surface from vaso-motor constriction, the goose-skin, erection of hair, polyuria, tendency to diarrhœa, and tremor."

Speaking of the influence of mental emotion as an excitant of epilepsy, Gowers† states:

"Of all the immediate causes of epilepsy the most potent are psychical—fright, excitement,

* "On the Influence of the Circulation on the Nervous System," 'Lancet,' 1881, vol. i, p. 648.

* 'Bristol Med.-Chir. Journ.,' 1906, vol. xxiv, p. 23.

† 'Epilepsy,' second edition, p. 25.

anxiety. To these were ascribed more than one third of those in which a definite cause was given. Of the three forms of emotion fright takes the first place. It is effective chiefly in early life, when emotion is so readily excited, and is most powerful at the transition from childhood to adult life, while after middle life it is almost inactive. . . . The female sex is notoriously the more emotional, and accordingly the disease results from fright in a larger proportion of females than of males. . . . It is also notorious that this difference between the sexes increases as life advances. In childhood one sex is almost as emotional as the other, but with puberty men become far less emotional than women. The influence of fright as a cause of epilepsy is in strict harmony with this fact. Under ten years of age the sexes suffer equally. Between ten and twenty the males suffer less than females, as 3 to 4; between twenty and thirty as 3 to 13; and over thirty the only cases due to this cause occurred in women."

When we reflect on the above remarks on the influence of fright in producing epilepsy, and on the fact that fright exerts a great influence on the cardiac and vaso-motor systems, and that a severe fright can cause a transient stoppage of the heart and even death, the evidence points strongly in the direction that the convulsions of infancy must depend on an affection of the cardiac and vaso-motor systems, and that the immediate factor in the attack is either a cardiac arrest or a cardiac failure so severe as to give rise to rapid failure in the cerebral circulation.

The convulsions met with at the onset of acute infections in childhood are worthy of mention. Under similar conditions rigors are common in the adult, so much so that it is almost an aphorism that a convulsion in a child is the equivalent of a rigor in an adult. I have, however, once seen a convulsion at the onset of pneumonia in a non-epileptic adult.

A rigor is associated with marked cutaneous vaso-constriction, with pallor and sensation of great cold. The sensitive cardiac and vaso-motor systems of the child may not be able to adjust themselves to a severe vascular crisis, and it is to be noted that the old-established method of cutting short convulsions in infancy by means of immersion in a warm bath by producing vaso-dilatation of the skin lowers the blood-pressure and relieves the heart.

Jacksonian Convulsions.

Local stimulation of the cerebral cortex by the electric current, or by the presence of a cortical tumour, are both competent to produce that type of convulsive seizure commonly known as Jacksonian. The muscles first involved in the convulsive movements are those related to the area stimulated, but the spasms rapidly spread to other groups, and finally the whole musculature of the body may be involved. Consciousness is not always lost in these fits, and if lost, only late in the course of the fit. The spread of the convulsion to muscles other than those related to the area stimulated indicates that a progressively increasing area of cortex becomes involved. Several possible explanations of this march of events must be considered.

(1) It might be due to a spread of the current; but if so one would expect that the spread should occur at the moment of application of the current, and moreover, the fact that areas very remote from the one primarily stimulated are involved—for instance, the opposite side of the brain—renders such an explanation very improbable.

(2) To a spread of the excitation, the view commonly held. That the area of musculature involved in the convulsive movements gradually widens is proof that the excitation spreads, but it affords no explanation as to *how* it spreads.

(3) It might be due to a spreading vaso-constriction of the cerebral blood-vessels, the resulting anæmia bringing about the spread of the convulsions. I have referred above to evidence suggesting that the cerebral vaso-motor mechanism is a much more active one than is generally assumed, and I would draw attention again to Harvey Cushing's observation that faradic stimulation of the cortex can produce a paling of the grey matter. It might be urged that if this were of common occurrence it should have often been observed, but it might easily be overlooked, for slight paling of a surface is not a very obvious alteration.

Sir Victor Horsley* was on one occasion operating on the cortex when the patient had an epileptic fit. He noted that the cortex became distinctly *hyperæmic during* the attack. This it would do as the result of the convulsions forcing

* Horsley, "Origin and Seat of Epileptic Disturbances," 'Brit. Med. Journ.,' 1892, vol. i, p. 693.

blood upwards through the great veins of the neck into the brain. The increasing venosity of the blood would also deepen the colour of the cortex, and moreover attention would in all probability not be attracted by any paling of the cortex but by the convulsions, when hyperæmia would occur almost immediately.

The phenomena of Jacksonian fits dependent on tumour might be susceptible of the same explanation, viz. a spreading vaso-constriction; but it is certainly difficult to correlate them with cerebral anæmia, and the possibility that they depend on a different mechanism must be admitted.

The Symptoms following upon Sudden and Prolonged Cerebral Anæmia.

So far we have considered the results following sudden and very transient cerebral anæmia. The symptoms resulting from a more prolonged arrest of the cerebral circulation are not less interesting. I have recorded two cases in which death occurred three and five days respectively after puncture of the chest. I will briefly note the salient features of these two cases:

Case 1. *Broncho-pneumonia and pulmonary collapse; exploration of lung with hypodermic syringe; collapse and convulsions; death five days later.*—F. J. S—, female, æt. 7 years, admitted into St. Thomas's Hospital March 7th, died March 13th, 1898.

On March 8th, at 11.30 a.m., an exploring needle was inserted into the right base. During the exploration the child lost consciousness, was stated to become very pale on the right side of the face, and also slightly cyanosed. Ether was injected subcutaneously and stimulants administered. At 1.30 p.m. she had a convulsion, and convulsions occurred frequently during the afternoon.

On March 9th her pulse was 132 and weak, head retracted, and she was still practically comatose.

By the eleventh the retraction of head had almost disappeared; she was irritable, resented all interference, and passed her evacuations into the bed. She remained unconscious and died on March 13th.

Post mortem.—The special feature of the appearance of the brain was its vascularity. There were a few small superficial hæmorrhages in the pia mater and the vessels over both hemispheres were much injected. On section the white matter had a pinkish colour, and there were numerous red spots where vessels had been cut across. The lateral ventricles were undistended and contained no excess of fluid. The vessels at the base and in the Sylvian fissures were healthy.

Case 2. *Old pulmonary tuberculosis; chronic left basal pneumonia; exploratory puncture; syncope, convulsions, left hemiplegia; death three days later.*—J. R.—, male, æt. 52 years, under the care of Dr. Acland at Brompton Hospital; admitted June 14th, died June 17th, 1890.

On examination the physical signs were suggestive of a localised collection of fluid at the left base. A puncture was therefore made just under the angle of the scapula. The needle was inserted for about an inch and a half, and seemed to penetrate a solid substance; no fluid being withdrawn, a second puncture was made one intercostal space lower. On asking the patient if it gave him any pain he replied quite naturally, "I hardly felt it;" he then almost immediately passed a large quantity of urine, turned pale, and fell backwards. Respiration ceased entirely at once; the heart beat most irregularly and spasmodically, and the radial pulse was not to be felt. Ether was injected subcutaneously, the interrupted current was applied, and artificial respiration was maintained for half an hour. He then had a fit in which the left arm became firmly flexed at the elbow, the thumb flexed into the palm, the fingers over the thumb, and the hand flexed at the wrist. The left leg was not affected. The eyes were deviated to the right and the pupils widely dilated. When examined a few hours later he was still unconscious. The left side of his face was slightly less wrinkled than the right; the left arm at times moved slightly, and then would become rigid and flexed; the left leg was rigid, the knee-jerk was exaggerated, and ankle-clonus was obtained with difficulty. The right arm was moved up and down occasionally.

On the morning of June 15th his pulse was 150. There was now obvious left hemiplegia, with much twitching of the muscles of the left side of the thorax and abdomen. In the evening the right arm was rigid and flexed, the right leg was extended and constantly twitching; ankle-clonus was obtained on both sides—more briskly on the right. The urine contained a trace of albumen.

On the morning of June 16th he was still un-

conscious. The left hemiplegia still persisted; the right arm was rigid with clonic spasms; ankle-clonus was absent, and the knee-jerk could not be elicited on either side. Several convulsive seizures occurred during the evening. The left optic disc was apparently swollen and blurred, with one flame-coloured patch; the right cornea was hazy, and the disc looked blurred. Death occurred three days after the onset.

Post mortem.—The pia mater generally was slightly opaque. The dura also was slightly thickened, but there were no morbid adhesions. The vessels at the base of the brain were healthy. The brain tissue was fairly firm, and no obvious lesion could be detected in any part.

It is unfortunate that no microscopical examination of the brain was made in either case.

In a case recorded by Hubert Armstrong,* the initial symptoms were those of complete cardiac inhibition, but recovery occurred in a few hours.

Several cases presenting similar features are on record in which the symptoms followed pleural lavage.

Dr. Cayley† reports one in which death occurred from washing out the pleura after operation for empyema. On one occasion the patient "became deadly pale, his arms stiffened, and his pulse became very slow, his pupils were widely dilated, and his breathing gasping. . . . The patient, who was profoundly unconscious, now became flushed, his pulse and breathing extremely rapid; he had convulsive tremors of the right arm and leg, the hand was clenched and the arm rigidly flexed; the left limbs were also rigid and extended. The head was sometimes turned to the right, sometimes to the left; the eyelids were closed, the eyeballs were constantly rolling from side to side, and there were spasmodic twitchings of the muscles of the right side of the face. The pupils were widely dilated and insensitive to light; the patient's body became bathed in a profuse sweat, and the temperature rose rapidly. . . . He remained unconscious with general convulsive twitchings, and died sixteen hours after the seizure."

Post mortem.—"The brain and its membranes appeared quite normal; no thrombosis or embolism of the sinuses or arteries could be discovered. Portions of the medulla were submitted to microscopical examination but nothing abnormal was discovered."

Dr. Goodhart* records a similar case in which death occurred nine hours after onset. A girl, æt. 16 years, was operated on for empyema, and the pleura washed out daily. On one occasion she suddenly turned livid and fell back. She ceased to breathe and no pulse could be found at the wrist; no convulsive fit occurred. Artificial respiration was immediately commenced, and in ten minutes respiration was re-established and the pulse could be felt feebly at the wrist. She was perfectly insensible and never recovered consciousness in the slightest degree. An hour after the attack the right side of the face and the right arm and hand were very blue and congested; this subsequently disappeared. Urine and fæces were discharged involuntarily soon after the attack commenced. Both arms were contracted and rigid. There was no paralysis or rigidity of legs. Transient paralysis of the right side of the face occurred. Both arms were moved about alternately. Death occurred nine hours after the onset.

Post mortem.—The brain and spinal cord were found to be quite healthy. The membranes, sinuses and vessels were searched without finding any evidence of thrombosis or embolism.

Raynaud describes a similar case† of a man, æt. 27 years, in whom daily lavage of the pleura was being carried out for empyema. On one occasion the patient collapsed, became extremely pale, with convulsive movements of arms; he scarcely breathed, and the pulse was feeble and intermittent. After recovery in half an hour vision was obscured. The right papilla was surrounded by serous effusion, the veins were in some places much swollen, in others compressed and empty. The inner half of the disc was of a dull white colour, and the outer red and with blurred edge. On the left side the disc was pale. By the evening consciousness had returned but sight remained abolished.

On the same evening another lavage was performed but was again followed by an epileptic fit—

* 'Liverpool Med.-Chir. Journ.,' July, 1906, p. 110.

† Cayley, 'Clin. Soc. Trans.,' vol. x, 1877, p. 16.

* "Empyema and its Treatment," 'Guy's Hospital Reports,' 1877.

† "De la mort subite dans la thoracentèse et des convulsions epileptiformes à la suite des injections pleurales.' 'Gaz. des Hôp.,' 1875, p. 1068.

severer than the first—and this was succedeed by a state of stertor absolutely similar to that of ordinary epilepsy. This lasted several hours, and then a series of epileptic fits occurred terminating in death.

Post mortem.—Nothing abnormal was found in the brain. Further, the patient had never suffered from any convulsion before.

Raynaud regarded these cases as not being epileptic (idiopathic) but as being due to the injection into the pleura, and attributed the syncope to a reflex vagus cardiac arrest, or to a reflex cerebral vaso-motor constriction involving the medulla.

Vallin* records the case of a man, æt. 23 years, with daily irrigations for empyema. On one occasion, and at the end of the lavage, sudden syncope occurred. Rigidity of limbs, coldness of extremities, and cyanosis of face were present. After three quarters of an hour opisthotonos. Death twelve hours later without recovery of consciousness. Post mortem *nil.*

Cayley further quotes a case of Lorey's in which after recovery of consciousness the ocular fundi were examined; the retinal arteries were found to be much reduced in calibre, the veins in part dilated and congested. In this particular case a further washing out of the pleura was followed by convulsions and death as in the above cases.

Post mortem.—Nothing was found in the brain to account for the condition.

The condition is fully described by Bouveret† who gives a full *resumé* of all cases up to 1888.

The causation of the cardiac arrest in these cases is of great interest. In some experiments‡ performed in conjunction with Professor Brodie, with the object of ascertaining which of the afferent fibres of the vagus cause inhibition of the heart when their central ends are excited, we found that the pulmonary fibres were by far the most effective in this respect. If the root of the lung be exposed in an animal and any of the pulmonary branches stimulated, a typical arrest of the ventricular contraction, as shown by the blood-pressure record, is produced. At the same time marked arrest of respiration occurs from excitation of the respiratory centre. The vaso-motor centre is also inhibited, and produces a further fall in blood-pressure, apart from that due to the cardiac inhibition, as proved by the fall in blood-pressure produced in an animal whose cardio-inhibitory fibres have been paralysed by atropine.

The subject has also been studied by Capps and Lewis* who concluded from experiments on animals with artificially induced pleurisy and from observations on the blood-pressure of man during aspiration of pleural effusions, that the pleural fibres of the vagus can give rise to a very active lowering of blood-pressure, and that this may be brought about either from a reflex vaso-motor depression or a reflex cardiac inhibition.

Similar Symptoms resulting from Prolonged Chloroform Syncope.

The conclusion that the cerebral manifestations in the above cases are due to prolonged cerebral anæmia is supported by the facts published by T. A. Green in his paper on "Heart Massage as a Means of Restoration in Cases of Apparent Sudden Death."† Numerous cases of recovery after chloroform syncope as the result of massage of the heart are on record, but in some, although the heart has been induced to beat apparently normally, death has resulted after a varying period with a train of symptoms indistinguishable from those noted in the above cases. The fact that in these cases of chloroform syncope the heart had ceased to beat for varying periods, and that therefore the cerebral circulation was for a time at a complete standstill, leaves no room for doubt but that the cerebral symptoms are to be attributed to the cessation of the blood-flow through the cerebral arteries.

Green's first case is as follows:

A boy, æt. 9 years, was being operated on for congenital umbilical fistula. During the early stage of the operation respiration stopped, "the lips became cyanosed, the skin pale and the pupils of the eyes widely dilated and insensitive. No pulse could be felt at the wrist and on auscultation no heart-sounds could be heard. The respiration

* "Convulsions éclamptiques à la suite de la thoracentèse," Vallin, 'Gaz. des Hôp.,' 1875, p. 1116.

† 'Traité de l'Empyème,' Paris, 1888.

‡ "On Reflex Cardiac Inhibition," 'Journ. of Physiol.,' 1900, vol. xxvi, p. 92.

* J. A. Capps and D. D. Lewis, "Observations upon Certain Blood-Pressure Lowering Reflexes that arise from Irritation of the Inflamed Pleura," 'Amer. Journ. of Med. Sci.,' 1907, vol. cxxxiv, p. 890.

† 'Lancet,' December 22nd, 1906.

continued spasmodically at intervals but finally stopped about five minutes later." All the ordinary means of restoration having failed, twenty-five minutes after the cardiac stoppage Dr. Green opened the abdomen under the left costal arch and commenced cardiac massage through the diaphragm. The apex of the heart was felt to be quite immobile and flaccid. Rhythmical compression of the heart was practised at a rate of about 70 per minute. After about two minutes a slight fluttering of the heart was observed and at the same time the pupils contracted slightly. Within a few seconds it began to beat with more than normal vigour at a rate of about 90 or 100 per minute. Artificial respiration had been continued all the time, and within a very short time of the restoration of the pulse spontaneous breathing asserted itself. Consciousness never returned, tonic spasms with rigidity of the limbs and trunk developed; he broke out into severe perspirations and the pulse and respirations increased in frequency. The muscular spasms were severe enough to necessitate the administration of morphia and chloroform. Death occurred twenty hours after the heart-beat and respiration had been re-established.

Green also records a second but less striking case occurring under his own observation, in which death occurred one and a half hours after the heart massage had been commenced.

Green reviews the literature and gives a synopsis of forty cases of heart massage for chloroform syncope, but for the purposes of this paper only those in which death occurred some hours after the heart failure will be mentioned.

Maag.* A man, æt. 27 years. Operation, nerve-stretching for sciatica. The patient became "asphyxiated" at the end of the operation. Ordinary measures tried for ten to fifteen minutes. The heart was exposed by the thoracic route, the third and fourth ribs being divided. Tracheotomy was performed and air blown into the lungs.

After a few compressions the heart began to beat, at first feebly, then more firmly. At the end of half an hour the first natural respiration was taken, but it was not until the end of three hours that these were deep and regular. Consciousness was never recovered, and the patient died eleven hours after the cardiac action had been re-established. During the last eight hours voluntary respiration was absent.

Gray.* Operation on a woman, æt. 55 years, for sudden asphyxia from laryngeal carcinoma. Tracheotomy was performed with artificial respiration. A few spontaneous respirations were taken but they soon ceased. After four or five minutes the abdomen was opened and the heart massaged through the diaphragm. It began to beat after four minutes, slowly at first, but gradually increasing in rate and strength up to 90 per minute. Artificial respiration was continued and gradually natural breathing was restored. Consciousness was never regained and the patient died three hours later. Cardiac arrest lasted about ten minutes.

Depage.† Woman; abdominal hysterectomy for fibroid. Chloroform syncope. Artificial respiration for fifteen minutes; then heart massage by the subdiaphragmatic route. The heart-beat was restored in a few instants; it was feeble at first but it soon became stronger. Spontaneous respiration did not return until one hour had elapsed. Consciousness was never recovered and she died after sixteen hours.

Ramsay.‡ Woman, æt. 27 years. Operation for prolapse of uterus. Chloroform syncope. Artificial respiration was commenced immediately. At the end of four minutes heart massage by the subdiaphragmatic route. Pulsation returned within a minute, at first feebly then becoming stronger, and spontaneous breathing soon followed. Three hours later the pulse was 168, irregular and intermittent. She slept for four hours and was at times delirious. On the next day she was better and she made a good recovery.

I have thought it advisable to mention in some detail the results following complete and prolonged cerebral anæmia, as though they have been described in the case of experimental ligation of the cerebral arteries in animals, they are not generally recognised as occurring in clinical medicine. In the next lecture I will continue this part of the subject, and also deal with conditions dependent upon increased intra-cranial tension with its resultant cerebral anæmia.

September 20th, 1909.

* 'Centralbl. f. Chir.,' 1901, p. 20.

* 'Lancet,' August 19th, 1905, p. 506.

† Depage, 'Journal de Chirurgie et Annales de la Société Belge de Chirurgie,' 1905, p. 238.

‡ Ramsay, 'Intercolonial Medical Journal of Australasia,' September, 1906.

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THREE CASES OF NERVOUS DISEASE IN WHICH THE DIAGNOSIS WAS DIFFICULT.

A Clinical Lecture delivered at St. Bartholomew's Hospital.

By J. A. ORMEROD, M.D., F.R.C.P.,

Physician to St. Bartholomew's Hospital and to the National Hospital for the Paralysed and Epileptic, Queen Square.

GENTLEMEN,—In the three cases which I shall bring before you, a question of great interest was that of diagnosis.

CASE 1.—The questions that arose concerning this patient were,—

(1) Had he some severe intra-cranial disease, such as effusion of blood, in consequence of injury? This appeared probable during the first day or two of his stay in the hospital.

(2) Was it a case of traumatic hysteria? Later observations of his case suggested this diagnosis.

(3) Was he a malingerer? There was some evidence of this also.

(4) Or were all these elements intermingled in the case?

He was at first in a surgical ward under the care of Mr. Bailey, and later of Mr. Bowlby, who kindly allow me to utilise their notes for the purposes of this lecture.

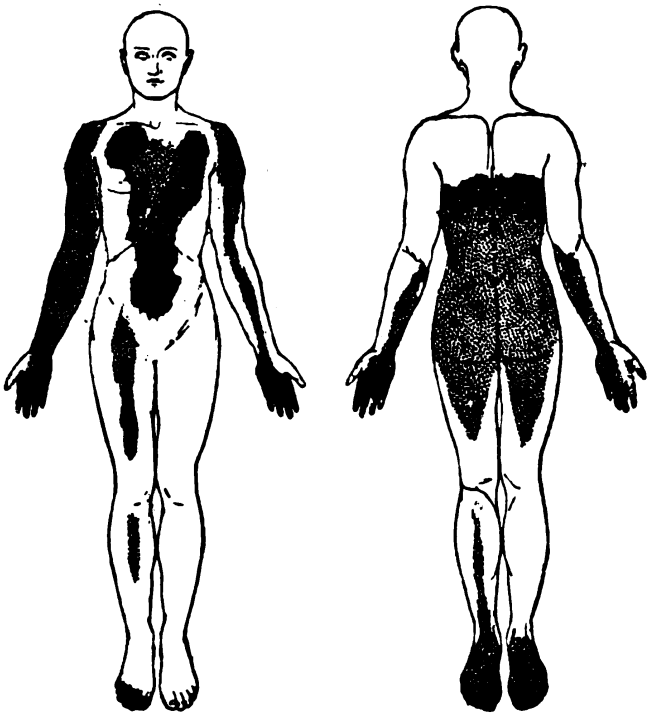
Frank B—, æt. 47 years, a labourer, formerly employed in South America, was admitted on June 29th, 1908, under the following circumstances:

He came to the surgery, complaining of pain in the abdomen and the left side of the pelvis, and of vomiting blood. He brought up in the surgery a little bright red blood. He stated that on June 27th he had been knocked down by a runaway horse; he went to one of the large hospitals, where his chest was strapped. Since then he had been at work.

On admission (at 2 p.m.) he was quite conscious

and there was no weakness of his limbs. At 3 p.m. drowsiness began, and this increased till at 3.30 he was quite unconscious. His limbs now seemed paralysed and flaccid. The respiration was diaphragmatic, somewhat spasmodic in character, 24 per minute, and accompanied by excursions of the larynx. There were movements (nature not specified) of the eyelids and eyes, and of the mouth and jaw. Food was swallowed. The pupils acted to light. The knee-jerks were active and equal; there was no ankle clonus. Most of the superficial reflexes were brisk, but no plantar response could

FIG. 1.



be obtained except in the tensor fasciæ femoris. There was retention of urine, and marked priapism occurred when a catheter was passed. The urine when drawn off was normal.

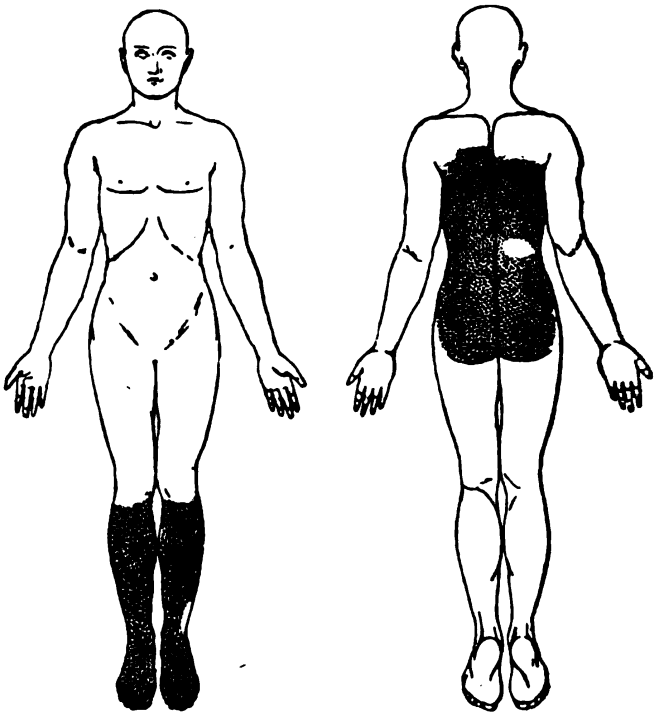
Mr. Bailey asked me to see him in consultation that afternoon, the questions being chiefly whether he had, as the result of injury, some effusion of blood on to the surface of the brain, and whether it was advisable to trephine. It was agreed not to trephine. The diagnosis seemed uncertain, and I ought to add that the possibility of hysterical coma did not then occur to me.

At 11 o'clock that night his condition was unaltered. At 1 a.m. lumbar puncture was attempted, but the patient straightened his back and showed signs of pain. At 3 a.m. he woke up and was able to answer questions. No previous history of fits nor of paralysis was obtained from him.

The next day (June 30th) he answered briskly and intelligently; he passed urine naturally. There was still some weakness of the arms and legs; and the respiration was diaphragmatic. The knee-jerks could not now be obtained.

There was extensive anæsthesia; general impairment of tactile sensation below the level of the eighth cervical vertebra, and absolute anæsthesia

FIG. 2.



over large areas; some of these corresponded fairly well to the distribution of nerve-roots (thus the soles of the feet were anæsthetic and the dorsa not), but others did not (Fig. 1).

July 2nd.—The knee-jerks were obtained again yesterday and to-day. Patient complains of a girdle pain at the level of the eighth and ninth dorsal vertebræ. The vision of the right eye seems greatly impaired; the field of vision in that eye is concentrically diminished; central vision for red, green and blue is lost.

July 9th.—There are some signs of recovery of motor power in the legs. The anæsthetic area on the trunk is diminishing, but both legs are anæsthetic below the knees, except a patch over

the left external malleolus; there is complete loss of muscular sense in the legs, and impairment of muscular sense in the arms (Fig. 2). The back is held rigid, the abdomen is distended, and there is still very little costal respiration.

On July 15th he is said have vomited a small quantity of blood-stained stuff.

From the time of his admission till July 11th (*i. e.* for nearly a fortnight) there were very considerable oscillations of temperature. Thus on June 29th and 30th the temperature rose from normal to 104° F. in a few hours, and sank as rapidly. On July 9th it rose to 105·5°, yet the pulse at these times was 64, and the respirations 20. Then came a normal period, and later on (in August, September and October), the temperature was moderately raised, reaching 100° or 101°.

July 28th.—Weakness of extensor movement in fourth and fifth fingers of right hand.

August 8th.—Blood in the urine.

September 2nd.—The anæsthesia seems to have dwindled to an oval patch on the abdomen, just to the left of the umbilicus.

At the end of October Mr. Bowlby asked me to see this patient again, and he was transferred to my ward on November 5th.

He was then unable to stand, though he could move his legs freely in bed. There was a certain amount of tremor and inco-ordination in the movements of his arms, but this did not inconvenience him. There was no sphincter trouble in evidence, though he was said occasionally to have retention of urine. The knee-jerks were normal; the plantar reflexes, though somewhat indefinite and difficult to obtain, were more flexor than extensor in type. The only remaining anæsthetic patch was that on the abdomen. My attention had already been arrested by the report of the anæsthesia which had previously existed. It appeared to have been too irregular and too extensive to have been the result of an organic lesion; and on examining the remaining patch on the abdomen, I found that it had a character which is often seen in hysteria. I am able to show you this now. If I touch or prick the anæsthetic patch (his eyes being closed) and ask him whether he feels it, he says "No." I next touch some sentient part of his skin several times, and ask him to say "Yes" each time he is touched, and he does so. I next ask him to say "No" each time he is not touched, and I touch the anæsthetic patch several times. He replies "No" with equal regularity. Evidently, therefore, he does feel, though he thinks that he does not. This little experiment suggested to me that the paralysis might also be hysterical. With this idea he was secluded behind screens, and faradised vigorously each day with the wire brush. In ten days (November 16th) he was making an attempt to stand, and he now (November 27th) can walk alone, though in rather a peculiar way. So that from the absence of any definite sign of organic disease, from the peculiar character of the anæsthesia, and from the rapid improvement during the last few weeks, I feel justified in diagnosing an hysterical paralysis. Was the disease hysteria from beginning to end? I cannot say for certain. It is possible; for hysterical paralysis does sometimes begin with an attack of coma, and it may, indeed often does, originate in an accident. Still I must own that this possibility did not occur either to Mr. Bailey or myself when we saw him in the state of unconsciousness.

And why have I mentioned the possibility of malingering? Not on account of the contradictory character of the anæsthesia which I have shown you, for that is very common in hysteria, and it would be an extremely stupid way of shamming; but on account of two other incidents which happened in my ward:

(1) On November 20th the nurse gave him the thermometer wherewith to take his temperature. It was found to be 107° F. Sister went at once and took it herself, and found it was 97° F. Then looking closely at the original thermometer it was seen that the index was separated into two parts—the inference drawn was that he had given it a shake. This was the only rise in the thermometer observed while he was in my ward, and I think that the charge of fraud is in this instance correct. I do not assert, however, that the temperatures in the earlier stages of his case were manufactured; indeed, looking over the charts taken on the surgical side, I do not think they were. Neither do I assert that variations of temperature, possibly extreme, may not take place in hysteria—that is another question, and a difficult one.

(2) His urine, which had been previously healthy (except, it would appear, on October 8th), was found a few days ago to contain blood. It was a reddish-brown, and had a considerable sediment just

like the urine of acute nephritis. The sediment, however, was found to contain no casts, but a quantity of squamous epithelium such as might have come from the interior of the mouth. We remembered that he had been bringing up frothy, blood-stained fluid from the mouth,* and it seemed probable that he had mixed this with his urine. But we refrained from cross-questioning him, as he had been extremely annoyed when questioned about the thermometer.

In these two instances, then, I think there was intent to deceive, though the bulk of his symptoms were genuine enough. Sometimes in hysterical cases (though not nearly so often, I think, as is commonly assumed) there is distinct malingering. I remember a woman in Queen Square with hysterical paraplegia who had on her back some scars, the result of old sores which had puzzled her previous medical attendent. She told us, in a moment of confidence, that she had produced the sores herself.

Case 2.—This is a case which I had the opportunity of seeing for the first time some nine years ago. The symptoms were then purely nervous, consisting partly of fits which appeared to be hysterical, partly of a mental defect of more durable character. I saw her again at the beginning of this year (1908); she was then gravely ill, with symptoms which I could not thoroughly explain, viz. retention (and suppression) of urine; breathlessness and cyanosis; œdema, petechiæ, and bullæ, and a state of semi-coma. Upon some of these latter symptoms the post-mortem threw considerable light, showing them to be due not to the state of the nervous system, but to an infection with consequent thrombosis.

F. A—, a single woman, æt. 35 years, was brought to me in August, 1899, by a friend who was in charge of her. From childhood she had been excitable. During the last eight years she had been very liable to forget things. During the last three years she had suffered from sudden "falls." When these first came on she had no warning, and there was no loss of consciousness. Lately she had had an aura, a sensation of pitching forward, and she was said sometimes to lose consciousness. After the attacks she brought up wind, and then was better. On one or two occasions lately she had laughed and screamed after the fall. She had an attack in my room, flung herself off the chair on to the floor, but did not hurt herself; her eyes were closed, her arms spread out, her back slightly arched. She did not lose consciousness, but could speak all the time. She drank water greedily afterwards. This attack seemed to be plainly hysterical, and the diagnosis was hysteria plus a peculiar loss of memory. I saw nothing more of her till March 8th, 1908, when Dr. Elliott Browne asked me to see her with him at her father's house. Dr. Browne has most kindly supplied me with an account of her case since I first saw her, which I here reproduce in abstract. In 1901 and again in 1905 she consulted him for dyspepsia and flatulence, which was on both occasions much improved by attention to her teeth. On February 10th, 1908, she complained to him of attacks of faintness and nausea, which were apparently relieved by a carminative. On February 20th, and again on February 22nd, more serious symptoms showed themselves, viz. attacks in which she became breathless, faint, and intensely cyanosed in her face and hands. On February 28th a further attack of cyanosis with hurried breathing, pain in the loins, scanty urine, slight anasarca of the legs, and a doubtful murmur at the apex of the heart. The next day (February 29th) there was pain in the legs as well as the back, and the urine became more scanty, till on March 4th there was complete suppression (catheter passed without result). The patient was apparently becoming comatose. Dry cups were applied to the loins, with the result that in an hour's time a large quantity of urine was passed into the bed. The same day a purpuric rash appeared on the right wrist and arm, and the next day (March 5th) on the abdomen and back; the buttocks became red and swollen. This state of things continued for the next few days, the urine being sometimes suppressed, sometimes retained, sometimes passed involuntarily. The temperature was at no time above 99° F.

When I saw her with Dr. Elliott Browne on March 8th she was in a stupid state, but not wholly unconscious. Her face was flushed, her tongue dry; the pulse was natural; there was a systolic murmur at the apex of the heart. The

* No definite hæmatemesis was ever observed, though he was said to have "vomited blood."

toes had a blue, congested appearance (the cyanosis passing off); there were spots on the abdomen which seemed to be the remains of the petechiæ; there were superficial sores on the skin of the groins and the buttocks. The knee-jerks were barely obtained. The plantar reflexes were not extensor. The bladder was distended to the level of the umbilicus, although she had passed urine four hours previously.

I was told that for many years she had been considered peculiar in her mind, very forgetful and very untruthful. A married sister was said to be very "jealous" and hysterical.

As proper nursing at home seemed impossible she was removed (March 10th) to St. Bartholomew's Hospital. The lethargic state continued; the pulse was at times irregular, there was still retension of urine, but no further suppression; the urine was pale, acid, sp. gr. 1016, and contained a trace of albumen.

March 13th.—Bullæ appeared on the toes.

March 14th.—The neck and the upper part of the chest became swollen and œdematous; nothing could be found, either externally or in the fauces, to account for this. In the afternoon she suddenly became cyanosed, her eyes fixed and staring, no pulse at the wrist; but after injection of strychnine and removal of mucus from the fauces she recovered, though death had seemed imminent.

March 15th.—The swelling of the neck increased.

March 16th.—There was a repetition of the attacks in which she became breathless and pulseless, but she recovered from them. There had been some signs of bronchitis in the chest, but now bronchial breathing developed at both bases, the breathing became more shallow, and she died. Just before death the temperature rose to 103° F.

The post-mortem was made by Dr. Langdon Brown, and there was found—

In the lungs, œdema, collapse of both bases with clear fluid in both pleuræ, and at the right base two large hæmorrhagic infarcts with patches of recent pleurisy on the surface. In the heart a large adherent ante-mortem clot in the right auricular appendix, and a large ante-mortem clot loose in the mouth of the pulmonary artery, and hanging down into the right ventricle.

In the colon, several patches of recent ulceration, the largest of which (near the valve) had an irregular outline, and a sloughy, thickened base.

The kidneys were not strikingly abnormal, but there was some thickening of the capsule, and the cortex was somewhat narrowed.

Both Dr. Langdon Brown and Dr. Andrewes considered the above appearances to be connected with some infection, and from the blood taken from the heart a cultivation was made of the *Bacillus coli*.

In the brain there was atrophy of the convolutions at the apex of both temporo-sphenoidal lobes and at the anterior parts of both frontal lobes. The spinal cord in the lumbar region down almost to the cauda equina was softened to a pulp.

Dr. Hinds Howell kindly undertook the further examination of the brain and cord and reported as follows:

The softening of the cord is to be regarded as a post-mortem change, since no evidence of myelitis could be obtained by microscopical examination.

There was slight matting and thickening of the pia arachnoid over the interpeduncular space of the brain; otherwise the cerebral meninges were quite normal, even over the sclerosed convolutions.

In certain areas of the brain the convolutions were shrunken, hard and tough, and the fissures proportionately wider. The distribution of this sclerosis was symmetrical, but perhaps more marked on the left than on the right side. It was most marked in the anterior part of both temporo-sphenoidal lobes and in the anterior and posterior thirds of the hippocampal gyrus. It involved also the anterior poles of both frontal lobes, and their orbital surfaces, and both islands of Reil and to a less extent their parietal opercula. There was nothing to show how it originated, and it was impossible to say whether it was a primary or secondary condition. Microscopically the sclerosed cortex showed a dense proliferation of neuroglial tissue, with atrophy and destruction of nerve-cells.

The permanent impairment of this patient's mental faculties may be reasonably connected with the atrophy of her cerebral convolutions, especially as the anterior parts of the pre-frontal lobes were atrophied; and it seems not improbable that with an enfeebled brain of this kind there should be associated such symptoms as hysterical fits. The nature of her last illness I was unable, during her life, to explain. At first, looking to her past history

of neurosis, I thought that perhaps the lethargic state and the retention of urine might have a purely nervous origin. It seemed, indeed, unlikely that the œdema, the cyanosis, and the purpura were due to such a cause, though even these symptoms have been described in connection with hysteria. But it soon became clear that some much more serious influence was at work, and I presume that, as suggested by our pathologists, this influence was a blood-infection. The purpura, the bullæ, and the thrombosis would be explained in this way, and recurrent attacks of dyspnœa, cyanosis and cardiac failure might be due to partial obstruction of the pulmonary artery by the loose clot. Still it is remarkable that an infection as virulent as this should not have given rise to a higher fever (the temperature before admission was never more than 99° F., nor after admission more than 101° until just before death), and that the illness should have lasted for over three weeks. The retention of urine, and the incontinence of urine (and, during the last few days, of fæces also) must, I suppose, be connected with the patient's lethargic and semi-comatose condition, seeing that the softening of the lumbo-sacral region of the cord was ultimately pronounced to be a post-mortem change. The anuria observed before her admission to the hospital I cannot account for.

Case 3.—This was a case of cerebral tumour, situated in the right frontal region. The patient on admission was evidently suffering from some serious nervous disease, but there was nothing in her physical condition to indicate the exact nature of it.

Some points in her history, viz. long-standing headache and the occurrence of some kind of fits, suggested, however, that the disease was within the cranium.

The occurrence of left-sided paralysis on the day before her death pointed towards the right side of the cranium. So that the discovery, post mortem, of a tumour in the right frontal lobe was not exactly a surprise, though the evidence, during life for the mere existence of a tumour, and still more for its localisation, had been exceedingly scanty.

Mary B—, æt. 42 years, married, was admitted to John Ward on October 28th, 1908.

She was in a stupid state on admission, the degree of consciousness varying from time to time; sometimes she was half comatose, sometimes she could understand and give an account of herself.

The history had to be pieced together from her own statements and those of her relations, and was very difficult to obtain.

There appeared to be no reason to suspect syphilis; she was said to be a hard-working woman, healthy except for her present illness, and only a moderate drinker (though a very furred tongue and some tenderness of the calves raised some suspicion as to alcoholism).

In April, 1907, she had an operation for piles, and she appears to have had some trouble with the sphincters since.

A year ago she had a blow on the head.

Ten months ago headaches began.

Two months ago she attended at a hospital for nervous diseases, apparently on account of headache and general depression.

During this last two months, also, she has had what she calls "funny feelings" (? a kind of *petit mal*), *i. e.* she used to lose herself when talking and then recover after a few seconds. She was said to have bitten her tongue occasionally. At this time she was still going about, but could not be trusted alone on account of these feelings.

October 22nd (*i. e.* six days before admission).—The headache got worse and she felt as if the head were opening and shutting.

October 23rd.—She began to be "stupid" and did not recognise people.

October 24th.—She refused to take food.

October 27th.—She is said to have lost consciousness altogether," and to have been "light-headed," but with moments of clearness.

October 28th.—She was brought for admission in a drowsy, semi-conscious condition. She complained on admission (in her more conscious moments) of pain in her head and in her chest. Her tongue was thickly furred; she had bad teeth and much pyorrhœa; her heart and lungs were normal. The liver could be felt about one and a half inches below the ribs, otherwise her abdomen was natural. She could move all her limbs. The pupils and ocular movements were natural; there was no affection of any cranial nerve. *There was no optic neuritis.* The knee-jerks were brisk; there was no ankle clonus, the plantar reflexes were flexor in type. I find no note of the abdominal reflexes; if

I remember rightly, they could not be obtained on either side. The urine was mostly passed underneath her, but when obtained a trace of albumen was found in it. Owing to her mental condition the sensation could not be properly tested.

October 30th.—Involuntary movements of the fingers are noticed from time to time, not tremor, but rather twitching movements. Both hands are affected by it.

November 6th.—She keeps moving her left hand to her chest as if to rub it; she has complained of pain there. *The right pupil is now larger than the left.* The breathing appears to be mainly diaphragmatic.

9.30 p.m.—She has had an attack in which breathing stopped altogether for ten seconds. She became dusky, but recovered again. *The left arm and leg now seem to be paralysed.* There is some twitching of the left thumb.

November 7th.—She is now quite unconscious; she cannot swallow, and has to be fed by the nasal tube.

4.30 p.m.—Her breathing again became bad and her colour dusky. Then her respirations suddenly dropped to five per minute, and eventually one per minute. The heart continued beating for two minutes after the breathing ceased.

The post-mortem was made by Dr. Langdon Brown. The organs of the chest and abdomen were natural, except the kidneys. The right kidney weighed 7 oz., and was slightly granular; the left kidney could not be found. In the brain there was, in the lower part of the right frontal tube, a soft, vascular growth, reaching backwards nearly to the Sylvian fissure. I show you a horizontal section of the brain, and you will see in the right frontal lobe a cystic cavity (quite distinct from the lateral ventricle). This cavity contained clear, yellow fluid. The posterior wall of the cyst was formed by soft, irregular growth, which apparently occupied the whole of the corpus striatum and lay entirely external to the internal capsule and lateral ventricle. Microscopically, this tumour is a mixed-cell sarcoma, containing multinucleated giant cells in large numbers.

It is worth while considering in the light of this post-mortem how far the case presented such symptoms as are thought to characterise a frontal tumour. For recent accounts of these symptoms I would refer to Dr. Grainger Stewart's paper in the 'Lancet,' November 3rd, 1906, and Dr. Beevor, "Lettsomian Lectures," 'Transactions of the Medical Society,' vol. xxx, pp. 173–188.

Of the three cardinal and general symptoms of cerebral tumour—viz. headache, vomiting, and optic neuritis—the last two were absent, although the tumour was a large and rapidly growing one. Headache had been present all through; I do not think we made out from the patient that it was localised to any one part of the head. Fits, apparently of the nature of *petit mal*, were mentioned in the history, and while these suggested a cerebral lesion they did not serve to localise it. Mental change was certainly present, but at the time of admission could hardly be described in detail, as the stupor was too far advanced. There was also involuntary micturition—a symptom on which Beevor lays some stress; but this may have been simply due to the stupid, mental state. There was none of the fine tremor of the hands which Grainger Stewart describes; no paralysis of cranial nerves so far as could be made out; no alteration of superficial or deep reflexes. And the only two symptoms which were in any degree localising, namely the dilatation of the right pupil and the paralysis of the left arm and leg, appeared only on the day of her death. So that a precise diagnosis during life was not made.

September 27th, 1909.

THE experiences at Chiari's and Schauta's clinics at Vienna with nfty-nine cases of laryngeal tuberculosis in pregnant women confirm the unfavourable influence of gestation on a tuberculous process in the larynx. Küttner has declared that a pregnancy in women with laryngeal tuberculosis is equivalent to a death sentence in 90 per cent. of the cases, and the reported experiences are even more discouraging: none of the thirty-two women with diffuse laryngeal tuberculosis survived the puerperium. In another group of eleven cases the laryngeal process, originally very mild, became transformed during pregnancy into the diffuse form, fatal in all. On the other hand, in some of the patients in whom abortion was induced the laryngeal process promptly took a turn for the better. In 20 per cent. of their cases spontaneous abortion occurred and these women all died. Of the thirty-two women delivered at term 60 per cent. of the children survived only a few days.—*Journ. A.M.A.*, vol. liii, No. 6.

SOME DISORDERS OF THE CEREBRAL CIRCULATION AND THEIR CLINICAL MANIFESTATIONS.*

By ALFRED E. RUSSELL, M.D., F.R.C.P.,
Physician to Out-patients, St. Thomas's Hospital.

LECTURE III.

MR. PRESIDENT AND GENTLEMEN,—In the last lecture we were considering the clinical symptoms following upon prolonged cessation of the blood-flow through the brain, as found in cases of cardiac syncope following exploratory puncture of the lung and lavage of the pleural cavity, and in cases of chloroform syncope in which the cardiac action had been restored by direct massage of the heart after prolonged arrest.

The subject has been studied experimentally by various observers. The blood supply to the brain of animals has been cut off and the effects produced on allowing the circulation to return have been studied. One of the most exhaustive studies has been made by Messrs. Stewart, Guthrie, Burns and Pike.† Their experiments were performed on cats. The animals were anæsthetised with ether; ligatures were placed round the innominate and the left subclavian artery proximal to the origin of the vertebral artery, the blood-flow being stopped by traction on the ligatures. Artificial respiration was kept up.

The extent of anæmia was tested by means of intra-venous injections of indigo-carmine in animals allowed to die without restoration of the cerebral circulation. It was found that anæmia of the brain and medulla was complete; no trace of pigment was ever found above the calamus scriptorius and usually none above the third or fourth cervical vertebra.

There is, however, an important distinction between their experiments and the results obtaining in the cases described in the last lecture. In the experiments the blood-flow was cut off from the brain and medulla only, the circulation in the greater part of the cord and in the trunk and lower extremities remaining; whereas in the clinical cases the whole circulation of necessity came to an end.

The observers noted the effects produced on the blood-pressure, pulse-rate, respiration, reflexes and muscular movements.

The light, lid and corneal reflexes vanished almost immediately after occlusion. The pupils dilated in from ten to sixty seconds. When dilatation began it rapidly developed, the maximal dilatation being attained in from four to five seconds. Then the cornea became lax, sunken and furrowed, indicating the reduced intra-cranial pressure.

Muscular movements.—There was usually a sudden stiffening of all the muscles following occlusion, with violent movements of fore and hind limbs and tail. Micturition and defæcation might occur. Then the fore-limb movements ceased; shortly afterwards the hind limbs relaxed, and the whole animal lay limp and quiet until after the restoration of the cerebral circulation. Intra-venous injection of strychnine during occlusion caused spasms of abdominal muscles and of hind limbs, but not of fore limbs, indicating that the anterior part of the cord had been rendered anæmic.

The cerebral circulation was allowed to return after varying periods and the effects noted.

Respiration.—The first sign of returning vitality in the respiratory centre was a strong gasp. This was repeated at progressively shorter intervals until spontaneous breathing was established. The first gasp might occur at a long interval after the restoration of the circulation. Thus, after an occlusion of twenty-eight minutes the first gasp occurred forty minutes after release.

The return of the reflexes was inconstant; thus the light reflex might not return for two or three days.

Convulsions.—"Convulsions varying in severity from occasional twitchings of the limbs to extreme opisthotonos and violent struggles of tonic or clonic type sometimes begin before the full return of the reflexes. Occasionally the cat may lie quiet for one to three hours before the convulsions begin. The head may be drawn back in extreme opisthotonos or may be bent downwards with the back convex. There may be tonic spasm of the fore limbs and

* The 'Goulstonian Lectures,' delivered before the Royal College of Physicians.

† "The Resuscitation of the Central Nervous System of Mammals," by G. N. Stewart, C. C. Guthrie, R. L. Burns, and F. H. Pike, 'Journ. of Exp. Med.,' 1906, vol. viii, p. 289.

clonic spasms of the hind limbs. Again there may be violent clonic spasms in which the animal flings itself about from one side of the room to the other. The convulsions may follow in such rapid succession as to make it difficult to distinguish any interval between successive seizures. At other times intervals of five to twenty minutes elapse between any two convulsions. The pupils dilate widely between the spasms. Stroking the fur, clapping the hands together near the animal's ear, etc., may throw the animal into spasms. The period of frequent and violent spasms lasts from two or three hours to as many days." Severe convulsions may terminate in death twelve to thirty hours after their onset.

Transection of cord.—Division of the cord in the upper dorsal region between the third and sixth dorsal vertebræ, if done before fairly complete recovery of the cerebral centres, is followed by collapse, cessation of respiration, cardiac failure and death. The integrity of the spinal centres is necessary for the resuscitation of the cerebral centres. Division of the cord after the spasms are well established is followed by transient shock, recovery and cessation of the spasms in the hind limbs; hemisection produces cessation of the spasms in the hind limb of the same side.

After the convulsive stage is over the animals may recover completely or they may partially recover, but with loss of intelligence, dying after a variable period.

The Deportment of the Animal in the Post-Convulsive Stage.

(a) *Complete recovery* has occurred after occlusion of 5, 6, 8, 9, and 16½ minutes.

(b) *Partial recovery.*—One animal after occlusion of ten minutes recovered with loss of intelligence, the life of reflexes alone persisting. It had to be killed on the fifteenth day on account of puerperal infection. The convulsive movements persisted for three and a half days.

On the fourth day it could assume a half-sitting posture.

Sixth day: Walked clumsily, cleaned its paws, purred when stroked, took food for the first time, having been fed by the tube prior to this.

Seventh day: Walked in a circle, bumping against things.

Twelfth day: Four kittens born, paid no attention to them unless one was put near her, when she would fondle and lick it.

Fourteenth day: Seemed blind and deaf.

In another animal eight minutes' occlusion was followed by paralysis of one fore limb. There were occasional convulsions following violent attempts to move about in the later period. There was no loss of intelligence. Death on ninth day from accidental strangulation.

In another twenty-two minutes' occlusion; paralysis of one fore limb but no loss of intelligence; death from pneumonia on seventh day.

After long occlusion death usually followed in thirty hours or less, and in these cases no post-convulsive stage was observed.

The Time Limit of the Recovery of the Brain from Arrest of the Circulation.

In the experiments on cats no animal recovered after a longer period of occlusion than 16½ minutes, though in one case after 22 minutes' occlusion the animal recovered without loss of intelligence but with paralysis of one fore limb, death following, however, from pneumonia on the seventh day. But these experiments did not impose so severe a test as in cardiac inhibition in man—for the heart remained beating during the whole period of occlusion of the cerebral arteries, so that the life of the spinal cord and of the rest of the body was not interfered with. The integrity of the spinal cord was found essential to recovery, transection in the upper dorsal region being incompatible with the resuscitation of the cerebral centres. In the cases recorded in man the spinal cord suffered from the same arrest of blood supply as the brain, and though this might not be so severe an injury as transection, it would presumably materially diminish the chances of recovery. It is difficult to say for what period the brain can withstand the total arrest of its blood supply and the patient make a complete recovery.

The following table taken from Green gives details of nine cases in which recovery followed direct massage of the heart for chloroform syncope:

In a case recorded by Sencert, seven or eight minutes is recorded as the time during which the heart was completely arrested before direct cardiac massage was commenced. A disaster such as chloroform syncope is not conducive to accurate observations of time, and it is probable that the

Case.	Time of ordinary methods of resuscitation.	Time of restoration of heart from commencement of massage.	Time of restoration of breathing from commencement of massage.
Igelsrud	3–4 minutes	1 minute	—
Lane	Uncertain	1 or 2 squeezes	12 minutes
Gray	Uncertain	2 or 3 squeezes	—
Cohen	2 minutes	1 minute	—
Crile	His special methods commenced immediately	5 or 6 minutes	5 or 6 minutes
Sencert	7–8 minutes	5 minutes	7 minutes
Conkling	2 minutes	1 minute	—
Smith	3 minutes	1 minute	A few seconds after heart-beat had been restored
Ramsay	4 minutes	1 minute	Soon after heart-beat had been restored

heart gave some beats under the artificial respiration, etc., applied during this period; but it was motionless when massage was begun, and five minutes elapsed before its contractility was restored. Some blood would presumably be forced round the circulatory system during this five minutes, so that the full five minutes could not be added to the seven or eight.

In Ramsey's case four minutes elapsed between the cessation of the heart and the institution of cardiac massage, the heart recommencing to beat one minute later.

We are probably safe in assuming that about five minutes' loss of its circulation is the outside limit of time that the human brain can withstand and recover completely. In the experiments on cats, death without any return of reflexes followed an occlusion of 7½ minutes, the longest period of occlusion with recovery being 16½ minutes, and in all probability the cat would be more likely to recover after longer occlusion than man; further, as stated, the cats had the advantage that the circulation through the rest of the body and spinal cord was intact.

The heart itself even in man can of course withstand much longer periods of arrest and recover its contractility. This is shown in the next table, also taken from Green.

The longest duration of survival in these cases was in Green's patient, who lived for twenty hours. In the cases of surgical operations with chloroform syncope the patient has been exposed not only to

Giving Particulars of Eight Cases in which Heart Massage was Partially Successful.

Case.	Time of ordinary methods of resuscitation.	Time of restoration of heart from commencement of massage.	Time of restoration of breathing from commencement of massage.	Survival.
Maag	10-15 minutes	A few compressions	3 hours	*
Sick	45 minutes	30 minutes	30 minutes	24 hours
Crile	*Nil*	9 minutes (Crile's special methods)	12 minutes	2 hours
Crile	*Nil*, but at least 8 minutes elapsed without any attempts	16 minutes (Crile's special methods)	16 minutes	34 minutes
Gray	4-5 minutes	4 minutes	4 minutes	2 hours
De-page	15 minutes	A few instants	1 hour	16 hours
Lenormant	*Nil*	6–8 minutes	¾ hour	5 hours
Green	25 minutes	5 minutes	5 minutes	20 hours

* Breathing stopped at end of half an hour. Heart continued to beat for eight hours.

the action of chloroform and a surgical operation of varying length, but also to a second abdominal operation for the purposes of carrying out the cardiac message, so that there are more factors against recovery than in the cases quoted of simple puncture of chest wall, and these cases survived for three and five days respectively.

The Condition of the Brain.

In the case of puncture of chest, followed by death five days later, which I mentioned in my second lecture, vascularity of the brain was noted as a special feature; there were a few small superficial hæmorrhages in the pia mater, and the vessels over both hemispheres were much injected. On section the white matter had a pinkish colour, and there were numerous red spots where vessels had been cut across. The lateral ventricles contained no excess of fluid, and the vessels at the base and in the Sylvian fissures were healthy.

It is of course necessary to be very guarded, lest too great importance be attached to the degree of vascularity of a brain as observed on the post-mortem table, inasmuch as the position of the head is of importance in the distribution of the blood. It is also to be borne in mind that

owing to inadequacy of valves in the jugular vein blood is readily forced upwards to the brain during convulsive seizures. Further, Mott,* in describing the condition of the brain in animals in whom the cerebral arteries had been ligatured, states that "in most of these brains experimented on a striking naked-eye feature was the distension of the veins of the cortex with blood, and frequently there was sub-pial hæmorrhage."

In the other case of puncture of lung with death in three days, the dura mater was described as being slightly thickened but without morbid adhesions, and the pia mater as slightly opaque; the vessels at the base were healthy, the brain tissue was fairly firm, and no obvious lesion could be detected in any part. In Cayley's case no naked-eye changes were found in the brain. Portions of the medulla were examined microscopically, and nothing abnormal was discovered; but this was in 1877, before the perfection of histological methods. In Goodhart's case no naked-eye changes were found in the brain.

In these cases, then, there was no evidence of gross lesion, and the cause of the non-recovery of the cerebral functions must be sought in some change affecting the nutrition of the neurone. Mott has described changes in animals after experimental ligature of the cerebral arteries, and doubtless similar changes would occur in man. In the animals, however, the vessels were permanently ligatured, and any return of blood-flow would depend on the establishment of a collateral circulation. Mott noted in addition to alterations in the cells and increase of blood in the superficial veins, an increase of fluid in the perivascular lymphatics and general œdema of the brain, which he took to be proportional and compensatory to the diminution of the arterial blood. This he ascribed to the establishment of a collateral circulation to the medulla and a concomitant secretion of an excess of cerebro-spinal fluid from the choroid plexus, which "would account for the œdema of the brain, the dropsical condition of the cells and the dilatation of the perivascular lymphatics."

It is possible that œdema of the brain may, however, occur in some of the clinical cases as suggested by Raynaud's observation on his second case—vision was obscured and the right papilla was surrounded by serous effusion, the veins were in some places much swollen and in others compressed and empty—and by Lorey's case, in which the retinal arteries were much reduced in calibre and the veins in part dilated. Further, Leonard Hill* noted and figured the condition of the fundus in a dog in which he had tied the two carotids and the vertebrals. The veins were very large and the arteries exceedingly small; the disc was pale but not swollen. These observations suggest the presence of an increased intra-cranial tension such as would be produced by œdema of the brain, and are sufficiently striking to suggest the trial of the withdrawal of cerebro-spinal fluid by lumbar puncture in any future cases of this kind.

Convulsive seizures are a noticeable feature in these cases and would raise the intra-cranial pressure—a condition probably favourable to the passage of blood from the cerebral capillaries into the perivascular spaces.

Until further knowledge of the histological changes in the brain in these cases is forthcoming, the cause of the non-recovery must be attributed to injury to the neurons and possibly to cerebral œdema.

Review of the Symptoms.

The cases come under very different categories: first, sudden cardiac inhibition during puncture of chest or lavage of pleura; secondly, cardiac inhibition in patients already unconscious from the influence of chloroform; and thirdly, experiments on animals in which no cardiac inhibition occurs, the supply of blood to the brain alone being abolished.

In the first group the inhibition may be of varying degrees of intensity and duration:

(*a*) Sudden severe fatal syncope. Numerous cases as noted are on record.

(*b*) Sudden syncope followed by complete recovery after the most alarming symptoms, as in the cases recorded by Armstrong, Raynaud and Lorey. Suddenness of onset is very characteristic; there is absolutely no warning of the onset of trouble. The appearance is either that of sudden death with total disappearance of pulse, arrest of respiration and pallor of face, sometimes with transient rigidity of limbs, or short of that there

* "Croonian Lectures," Lecture II, 'Lancet,' June 30th, 1900.

* 'The Cerebral Circulation,' 1896, p. 140.

is sudden unconsciousness, gasping respiration, dilatation of pupils, extreme feebleness of pulse and cyanosis.

In one of Raynaud's cases the patient was completely unconscious for a quarter of an hour with involuntary micturition and defæcation: this state was followed for three quarters of an hour by stertorous breathing, and when consciousness was regained paralysis of the right arm was observed. Recovery took place in a few days. In Ramsay's case of resuscitation after chloroform syncope the patient was delirious before recovery took place. In Raynaud's second case there were convulsive movements of arms and recovery followed in half an hour. A second pleural lavage on the same day was followed by coma of several hours' duration succeeded by death after a series of fits. In Lorey's case the same alarming symptoms occurred and death also followed a second lavage—a strong warning of the risk attending a second interference with the lung or pleura in cases presenting such signs as cardiac shock.

(*c*) Sudden syncope; partial recovery, followed by death after varying periods of time.

This group may be compared with the cases occurring under chloroform anæsthesia in which the onset of symptoms is denoted by arrest of pulse and respiration, but with the resuscitation of the heart and with the disappearance of the effects of the anæsthetic these cases are identical save for the extra shock attending the surgical operation. They are also comparable to a considerable extent with the third group—the animals whose cerebral vessels were ligatured for varying times, save that in these the circulation through the rest of the body was maintained.

The onset.—The suddenness of onset is highly characteristic, and may be compared with the equally sudden onset of unconsciousness in the fit of idiopathic epilepsy.

Pulse.—This in some cases cannot be felt at the wrist, in others it has been noted as feeble or slow or intermittent.

Spasms: (a) *Initial tonic spasm.*—In the case of sudden death I reported tonic extensor spasm of arms was noted, with a convergent squint. In Cayley's case the patient's arms "stiffened." In Vallin's case rigidity of limbs was noted. This initial spasm is to be distinguished from the later convulsive movements, and would appear to be the direct result of the sudden cessation of the cerebral circulation. It probably occurs oftener than is recorded, as the extreme urgency of the cardiac failure in these cases is not conducive to observations of transient symptoms. In the cases of chloroform syncope the anæsthetic would doubtless negative the spasm. In the experiments on cats "there was usually a sudden stiffening of all the muscles following occlusion, with violent movements of fore and hind limbs and tail . . . Then the fore-limb movements ceased; shortly afterwards the hind limbs relaxed, and the whole animal lay limp and quiet until after the restoration of the cerebral circulation." The sudden stiffening is obviously the same phenomenon as the initial tonic spasm in man, the violent movements of limbs and tail probably depending on the fact that the spinal circulation was intact in the animals. (Leonard Hill noted the frequency of extensor rigidity when the limit of cerebral anæmia is reached and the excitability of the cortex is vanishing.) This initial spasm is seen in the tonic spasm observed after the unconsciousness and fall of the epileptic fit.

(b) *Clonic convulsions.*—These do not seem to occur in the cases of sudden and permanent cardiac inhibition. In the two cases I have seen, in one, the child with sudden death, only extensor tonic spasm of arms was observed; in the other, which occurred when I was syringing out the pleural cavity, the patient, who was sitting up in bed, fell backwards with absolute suddeness. There certainly were no clonic convulsions, and I do not remember whether any tonic spasm occurred.

Clonic convulsions in these cases appear to be conditioned by the return of the cerebral circulation. Their time of onset varies very considerably. They may appear very soon after the onset of syncope. In one of Raynaud's cases they occurred at the end of a minute, and in others they seem to have appeared very quickly, though exact observations of their time of appearance are naturally scanty. Or they may appear much later, as in the case of the child at St. Thomas's Hospital, in whom the first fit occurred two hours after the attack. Considerable variation was also noticed in the experiments on cats, in whom the convulsions might appear speedily after the release of the vessels from occlusion, or not for an hour or more. With a very long period of complete cerebral

anæmia the functions of the cortex and tracts must be permanently abolished. With periods of anæmia shorter than this the excitability of the cortex and the conductivity of the tracts revive on restoration of the circulation.

Subsequent course of these cases.—In addition to the symptoms already mentioned the pupils dilate and become insensitive to light. Involuntary micturition and defæcation occur. Severe perspirations are common. Consciousness does not return, convulsions may recur from time to time, the deep reflexes may be exaggerated, irregular movements or rigidity of one limb or of both limbs of one side may occur, hemi-anæsthesia may be detectable, and finally death occurs. In one case here recorded death did not occur till the fifth day. In the case of the cats definite dementia was noted in some cases following long occlusion of vessels. A similar condition has been observed by Leonard Hill in dogs and monkeys. It is conceivable that in man periods of cerebral anæmia of slightly shorter duration than those producing death might produce the characteristic symptoms of sudden syncope followed by a convulsive period terminating in dementia instead of death.

These cases of sudden and prolonged failure of the cerebral circulation are of great importance, not merely in that the clinical symptoms are of profound interest, but in view of the gravity of these accidents. They have also, I think, some bearing on the phenomena of epilepsy. Following upon a sudden arrest of the circulation, sudden syncope with unconsciousness is produced. In several cases transient tonic spasm was observed, and it may be that this is a common symptom. The first two symptoms of an epileptic fit are thus reproduced. Inasmuch as the arrest of the cerebral circulation in the cases just described was of very considerable duration, so long in fact, as to render recovery impossible, the subsequent symptoms of necessity differ from those of the transient epileptic fit. Clonic convulsions do, however, occur with the return of the circulation. The condition bears some resemblance to status epilepticus and a stronger resemblance to some cases of uræmia. It is unquestionably the result of the severe cerebral anæmia, and in the next section evidence will be given that both status epilepticus and uræmic coma and convulsions also depend upon the same factor.

(*To be concluded.*)

September 27th, 1909.

WITH DR. LEONARD WILLIAMS AT THE POLYCLINIC.

THIS man, æt. 43 years, has been in the wards of the Hospital, and he came last Friday to report himself. There is nothing very important in his history beyond the very significant fact that twenty years ago he had syphilis. On examining his præcordial region you will find that he has a left ventricle which is perhaps slightly enlarged, though not markedly so, and a double murmur of the see-saw variety at the aortic base, neither of the elements of which are, however, conducted down the sternum. The text-book conclusion at which to arrive under these circumstances is that he has aortic obstruction and aortic regurgitation. Such, however, to my mind would be an incorrect diagnosis. When I examined him before, I was able to persuade myself that his pulses were unequal in time. I do not think there is any doubt whatever that they are unequal in volume; but inequality in volume is not really a very significant matter. It could hardly surprise one to find that the right radial in the ordinary right-handed man was rather bigger than the left radial. Inequality in time, however—that is, when the two radial pulses are asynchronous—is a very different matter, the only causes which we recognise for such inequality being either something pressing upon one of the arteries leading to the part, or an aneurysm.

In order to test my impression that there was an inequality in time in this case I took sphygmographic tracings on the two sides within two or three minutes of one another, and you will see not only that the two are very different in type, but that so far from being a tracing of ordinary aortic regurgitation, one of them, that of the left side, is distinctly a tracing of aortic obstruction, because the wave, as you see, has the characteristic broad top. The observation showed that I was correct in my estimate of the inequality of time—a matter about which it is sometimes very difficult to be certain. An additional reason for setting aside a diagnosis of aortic regurgitation is that on neither side, to ordinary clinical examination, will you be able to detect the collapsing or water-hammer pulse, which was first described by Corrigan, and which is so characteristic of aortic regurgitation.

Neither will you be able, unless your eyes are much better than mine, to elicit any capillary pulse. The position, therefore, is this: although the patient has a diastolic murmur which is audible only at the base, and which should therefore, according to the text-books, indicate the presence of aortic regurgitation, he has none of the concomitant signs by which we recognise that condition. What, then, is the meaning of this see-saw murmur which is so plainly to be heard in this position, and which is conducted upwards rather than downwards? The systolic murmur which is heard at that spot is of course easy of explanation. It is commonly regarded as due to aortic obstruction. It is, as a matter of fact, far less significant of aortic obstruction than it is of aortic degeneration, and by aortic degeneration I mean, of course, calcareous degeneration of the first part of the aorta itself. When this portion of the great vessel degenerates, as after syphilis it is so very liable to do, calcareous plaques are deposited on the intima causing it to become rough. The passage of blood over this roughened surface creates a murmur which to our ears is identical in time with that which is caused by the narrowing of the aortic ring.

Now, when this calcareous degeneration takes place it is only one step further to a yielding, and consequent bulging, of the portion thus affected; so that, given a chronic aortitis, one of the results which must be expected is a bulging of the aortic arch and the commencement of an aneurysm. It is true that this degenerative process frequently spreads downwards so as to involve the aortic ring, narrowing it, and the aortic valves, puckering and rendering them incompetent, but I do not think anything of the kind has yet occurred here. I think the diastolic murmur, especially having regard to the fact that it is so rigidly confined to one portion of the chest wall, and that portion the one which lies above the aortic arch, must be due to some condition analogous to that which produces the systolic murmur—that is to say, there is probably already a bulging of the aorta and something in the nature of an eddy over the roughened intima which is sufficient to give rise to the diastolic murmur.

There is another fact which is strongly against the diagnosis of aortic regurgitation in this case, and that is that the patient's systolic blood-pressure is not more than 140 mm. Hg., which at his age cannot be considered an excessive figure. It is of course quite possible that the patient may develop both aortic constriction and aortic regurgitation, but at the present moment, his see-saw murmur notwithstanding, I make so bold as to say that he has neither. If the calcareous degenerative process spreads downwards, in the manner already indicated, and involves the aortic ring and the valves, this double valvular lesion will most certainly ensue. It seems to me, however, that the danger which really threatens him at the moment is that of an aneurysm. I have not yet had an opportunity of having him X-rayed, but I shall be surprised if, on the screen, it does not appear that there is a bulging of his aortic arch.

There is another thing which calcareous degeneration may do. As it spreads downwards it sometimes, and indeed not infrequently, travels along the coronary arteries, and we have all, in the post-mortem room, seen these vessels converted from elastic tubes into rigid stems resembling those of a clay pipe. This on the whole is the most serious result of the degenerative process, for with coronary arteries in that condition the patient is liable at any moment to instant death from angina pectoris.

The text-books are rather fond of multiplying types of angina pectoris, a habit which I think is the reverse of helpful. There is only one kind of true angina, the angina which is evoked by muscular exercise, which forces the patient to an immediate halt—nails him, as the French say, to the spot where he is standing. That is the angina which ensues as the result of calcification of the coronary arteries.

Now the commonest cause of this degenerative process is, as we all know, syphilitic infection. It also owns another cause which is not so well recognised. Persistent high blood-pressure, hyperpiesis as Sir Clifford Allbutt has called it, will produce precisely the same effect if allowed to go unremedied. In the one case, syphilis, you have the arterial wall so weakened that it cannot resist the impact of a normal blood-pressure; in the other, hyperpiesis, you have a perfectly normal arterial wall which is shaken and torn, so to speak, by the force applied from within. For we must remember that high blood-pressure exerts its most powerful influence at that part of the aorta which lies immediately above the valves. The difficulty

about these cases of hyperpiesis is that they seldom complain until the trouble is irremediable. People do not often come to consult one complaining of symptoms which immediately suggest high blood-pressure. It is only by asking for these symptoms, especially for the dyspnœa of slight effort, and by the routine use of the manometer that we can hope to detect the trouble in its early stage, and thus to save our patients from the disasters which unfortunately threaten this man.

In connection with this case I should like to show you the heart, large vessels and ribs from a case which I showed here last session. Many of you will remember him when I show you his photograph. He, too, had had syphilis, and I saw this aneurysm growing, so to speak, under my eyes for about two years. The patient was a hawker who wheeled a heavy barrow, and it was only just a month before his death that I managed to induce him to come into the hospital. You will see that the aneurysmal sac has eaten through two ribs, and has spared the origin of the innominate artery. There were practically no auscultatory signs during life. The aortic valves you see were practically intact, and death eventually took place by rupture into the œsophagus.

One interesting feature of the specimen is the size of the left ventricle. The text-books describe the left ventricle in cases of aneurysm as hypertrophied, and clinically it generally seems to be, because the heart's apex is displaced. The left ventricle in this case is not only not hypertrophied; one would rather describe it as smaller than normal, a fact which bears out what I have just said, namely that where syphilis is the cause of an aneurysmal swelling such aneurysmal swelling is due to primary degeneration of the artery, which yields in consequence to a perfectly normal, or it may even be a subnormal, blood-pressure. It is only where the aneurysmal swelling is due to the opposite condition of high blood-pressure acting on a normal arterial wall that the left ventricle may be expected to enlarge, and it enlarges, of course, not because of the aneurysm, but because of the increased peripheral resistance which must be overcome.

This woman, æt. 51 years, came to the hospital about four months ago complaining of œdema of both legs. The œdema was so considerable as at once to give rise to a very strong supposition that some form of mitral disease was in operation. However, the most careful examination failed to reveal anything at all abnormal with the heart or arteries. The liver was not enlarged, nor could any obstruction sufficient to account for the œdema be found by examining the abdominal organs. The blood-pressure was 165–170 mm. Hg.; the urine had a specific gravity of 1015; it was acid and contained neither albumen, sugar, nor granular casts.

Seeing that we can exclude heart disease, kidney disease, and mechanical causes of pressure within the abdomen, how are we to account for this œdema, which, though much less than it was, is nevertheless still very apparent? Well, if you will consider the age of the patient, which is fifty-one, and consider also what usually takes place at that age, I think we shall find a solution to the difficulty. Normal menstruation is an excretory act, and the function of the ovaries, apart altogether from ovulation, is that of supplying an internal secretion to the economy, which is in many ways comparable with the secretions of the supra-renal capsules and the thyroid. The climacteric, therefore, brings

about two changes; it closes up an excretory route which has been open for many years, and it suppresses an internal secretion to which the economy has for a long period been accustomed. It is a significant fact that the climacteric, however normally performed, is almost invariably accompanied by an increased blood-pressure. It is said that the internal secretion of the ovary is vaso-dilator in its effect, a fact which may or may not be true, though I believe there are some experiments supporting this view. This at any rate we can say, that the phenomena of the menopause, in causing on the one hand the retention of certain excrementitious matters, and, on the other, of withholding the internal secretion induce a disturbance which is reflected in the vaso-motor system. That this disturbance frequently shows itself in the form of œdema I have on several occasions been able to convince myself.

One case I remember particularly well, a case which I showed on more than one occasion at the cliniques at this College, was that of a woman, æt. 51 years, who, at the time when the period ought to have arrived, suffered from what is called intermittent hydrops articuli. One of her joints (it was generally a knee, and by no means always the same knee) became hot, swollen, and full of fluid. It presented, indeed, all the appearance and gave rise to all the symptoms of an acute synovitis of the joint. This condition lasted three or four days, and then gradually subsided, until at the end of the week she was perfectly well. This state of matters continued for about three years, the attacks, though perfectly regular, becoming less severe until at last they disappeared altogether.

Other cases of œdema of the lower extremities similar in kind to the one now before us I have also noticed, but I do not think that I have ever seen anything so severe as this woman's case when she first came to us.

Now the question of treatment of these troubles is of the utmost importance. It is not so much what to do as what not to do. If we must do something, and it is generally useful so to do, I find the best drugs are ovarian extract and ichthyol, combined with a diuretic such as theobromine, with mercury as an alternative. The *modus operandi* of the ovarian extract and the two last named is sufficiently obvious. How the ichthyol acts I cannot pretend to say, but that it does produce an extraordinary amelioration in the subjective symptoms which are liable to occur at the menopause I am able with very considerable confidence to affirm. For the rest, attention to the bowels and encouragement to the patients to be moderate in diet and to take plenty of exercise in the open air substantially comprise the therapeutic indications. It is what to avoid which is important. The presence of œdema to some medical men acts as a reflex, and they prescribe digitalis with the same promptitude as they contract their quadriceps extensors when their patellar tendons are tapped. Another drug which flows freely, and even eagerly, from the prescriber's pen is strychnine, and more often than not it is found in combination with digitalis. Now, on the face of things these two drugs may seem indicated in a condition such as that before us. The œdema, the complaints of faintness and debility, and disinclination for bodily and mental exertion all suggest a tonic, more especially a cardiac tonic. But it is a wile of the Evil One. Whatever else we may be ignorant of in connection with the menopause, this at least we do know, namely that it is frequently accompanied by high blood-pressure due to contraction of the peripheral arteries consequent upon retained toxins. The heart is labouring, it is true, but it is labouring under the burden imposed by the increased resistance. Under such circumstances to prescribe digitalis and strychnine is merely to add to the burden and to hasten, instead of providing against or delaying, the threatened catastrophe. For even in the absence of digitalis and strychnine catastrophes do occur, and their nature sufficiently proclaims their origin in high arterial tension. The so-called cardiopathies of the menopause, the tachycardias and the arhythmias, no less than the apoplexies, which are liable to occur at that time, are all due to the increased blood-pressure, which can only be made worse and more threatening by the careless exhibition of these powerful drugs. The process of the menopause is often protracted over years, and during such a period there is ample time for the development of that degeneration of the first part of the aorta to which I have already alluded in connection with the first patient and that of the post-mortem specimen. And with the aortic degeneration once established we are in full view of many very disquieting possibilities, of which aortic regurgitation is by no means the worst. It is not at all easy, even under favourable conditions, to prevent or arrest this degenerative process because the high blood-pressure of the menopause often proves very intractable to treatment. We can, however, see to it that we do nothing to aggravate matters, and from such complicity in evil-doing the use of the manometer in all these cases will certainly save us.

September 27th, 1909.

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A CLINICAL LECTURE

ON

THE OPERATIVE TREATMENT OF CARCINOMA OF THE UTERUS.

Delivered at the London Hospital.

By ARTHUR H. N. LEWERS, M.D., F.R.C.P.,
Senior Obstetric Physician, London Hospital.

GENTLEMEN,—I propose to-day to say a few words about the operative treatment of carcinoma of the uterus. But before coming to the actual treatment of that condition I think it will be an advantage if I say something in the nature of a few preliminary remarks about cancer of the uterus itself.

Preliminary Remarks.

As you probably know, cancer, in the sense of carcinoma, may begin either in the cervix or in the body of the uterus, and the ætiology of the disease is a very different one according as it starts in one or the other of these two positions. Carcinoma of the cervix is very much commoner than is carcinoma of the body of the uterus. The large majority of cases of cancer of the uterus which you will see will no doubt be cases of cancer of the cervix.

Cancer of the Cervix.

As regards the ætiology of cancer of the cervix there are certain points which it is necessary you should bear very clearly in mind. The first is that cancer of the cervix occurs in relatively young people. One is apt to associate the occurrence of cancer always with advanced age, and to think that only people of advanced or middle age are likely to be the subjects of carcinoma. But in the case of cancer of the cervix it is relatively common in comparatively young people. For instance it is not uncommon at the age of thirty, and we even find a certain number of cases—and I have seen a

few—in which it occurs under thirty years of age. But at and beyond thirty years of age it becomes fairly common, and the fact of a person being of that age does not militate against the likelihood that what she is suffering from is cancer of the cervix. In fact in some statistics I worked out when writing a monograph on the subject based upon my own cases, I found that the age-incidence of cancer of the cervix was practically the same in the decade thirty to forty as it was in the decade forty to fifty; there was very little difference indeed between the two. So much for the age.

Now we come to another important point, namely the number of children that these patients have had. The majority of cases of cancer of the cervix occur in patients who have had large families. Every now and then, as an exceptional thing, one may come across a case in a nullipara or in a patient who has had only one child; but as a rule patients suffering from cancer of the cervix have had several children. And on that point also I have worked out figures from my own cases, and the result was as follows: that no less than 47 per cent., taking the cases of cancer of the cervix, had had five children and upwards, and only 13 per cent., had had no children at all. For purposes of comparison I took a long series of patients, consecutively, turning over the pages of my case-book, cases which were not cases of cancer of the cervix. And I found that of these cases which were not cancer of the cervix, only 13 per cent. had had five children and upwards, and as many as 30 per cent. had had no children at all. If you compare these figures the difference is found to be very striking. 47 per cent. of the cases of cancer of the cervix had had five children and upwards, whereas only 13 per cent. of the other cases had had five children. So undoubtedly there must be some relationship—what it is we cannot be quite certain about—between repeated pregnancies and the occurrence of cancer of the cervix. It may be traumatism; it may be chronic inflammation, though it cannot be that entirely, because you have seen that it occurs occasionally in women who have never had any children at all. So that while frequent child-bearing is a predisposing cause, there must be some other cause at work which determines the occurrence of the disease.

I will now say a word or two about the symptoms of cancer of the cervix, and preface what I have to say on that by remarking that nothing is more lamentable than the way in which cancer of the cervix is overlooked in its early stages. No doubt in many cases that may be the fault of the patient herself. She may not seek advice, hoping that the symptoms may be due to something which is not of any very great importance. The symptom which more pre-eminently characterises the early stages of cancer of the cervix is bleeding, bleeding between the periods, or some discharge containing blood in between the periods. At that time there is no pain whatever in cases of cervical cancer. Remember that, because the public mind associates pain with cancer, and the patient is apt to think because she has no pain that, therefore, no matter what the trouble is, it is not likely to be cancer. But there is no more dangerous fallacy. For a long period, in fact as long as the disease remains limited to the cervix itself the patient has no pain at all. It is not until the disease begins to spread beyond the limits of the cervix that you begin to find the patient has pain. So do not be misled. Any unexplained bleeding, any bleeding occurring between the periods—if we take a patient during menstrual life, or still more definitely any bleeding occurring after a definite menopause has been established—is extremely suggestive of cancer. Of course, during menstrual life there are a large number of other diseases which also cause bleeding in between the periods, or what is called metrorrhagia; but bleeding occurring after the onset of a distinct menopause, such as the cessation of the periods for upwards of two years, is nearly always due to carcinoma beginning in some part of the genital tract. I should think more than 95 per cent. of the cases of bleeding after the menopause are due to carcinoma, either of the cervix, or of the body, or of the vagina. Therefore never be willing to let cases of unexplained bleeding pass by without insisting on a careful examination. As a rule the recognition of cancer of the cervix, when you do examine the case, is an easy thing. Cases which are overlooked are overlooked generally because they are not examined. Cases where there is much difficulty in making a diagnosis when an examination is made are very few. Among the suggestive things occurring on examination is free bleeding. You may occasionally see an erosion of the cervix which may have a somewhat suspicious appearance:

it may cause a little bleeding in between the periods, but the amount of bleeding on manipulation will be only slight; the bleeding in such cases is never considerable. But in cancer of the cervix even a quite gentle examination will cause free bleeding. Fresh bright blood will come away, producing a clot in the vagina, and thus interfering very much with the view of the cervix when a speculum is passed. Such a condition of things is very suggestive of carcinoma. The occurrence of hæmorrhage after coitus is another symptom extremely suggestive of cancer of the cervix. I said just now that there is no pain in the early stages. There is another thing which you should bear in mind, which is contrary to the popular impression of cancer. You do not find wasting of the patient as a rule in the early stages. Many patients with cancer of the cervix, even rather advanced cases, are quite stout, well-nourished women, and if you saw them just sitting among other cases, say in the out-patient room, you would very likely say that they looked the picture of health, and that there could not be very much the matter. I say again do not let that mislead you. Patients with cancer of the cervix may have no pain, they may present a healthy appearance, and be quite well nourished—not rarely even excessively stout. There is pain in the later stages of cancer of the cervix. Once the disease has spread beyond the anatomical limits of the uterus there is pain. But that is at a time when the disease has spread beyond the uterus into the adjoining regions, when at all events it is an unfavourable case; it may not be inoperable nowadays, but it is unfavourable. And even though at the present time more extended operations for treating cancer of the cervix have been devised, and are practised successfully, there is no doubt it is as important as ever it was, with the view of curing the patient, to recognise the disease at the earliest possible moment.

Cancer of the cervix may begin either on the vaginal portion of the cervix (the part which you see when you pass the speculum, and expose the upper part of the vagina), as an obvious projecting patch of growth, or as an ulcer, or as a nodule; or, on the other hand, it may begin in the upper part of the cervix, in the cervix proper. The growth on the vaginal portion is a squamous carcinoma. That which affects the upper part of the cervix, or begins in the cervical canal, in the substance of the cervix proper, is a glandular carcinoma.

Now as regards the direction in which this growth may spread. It may spread either downwards on to the vagina, it may spread upwards into the body of the uterus, and it may spread outwards, in every direction from the cervix into the connective tissue all round. Remember the cervix is surrounded by a connective tissue which in front separates it by an interval from the bladder, and passes off into the broad ligaments, and which posteriorly runs into the utero-sacral ligaments, and so towards the rectum. Into that connective tissue the carcinoma may spread. Once the disease is advanced it spreads there, and consequently gets to the bladder, and out from the broad ligaments into the utero-sacral ligaments, and ultimately involves the rectum. It may also involve certain glands. The glands which are involved in cancer of the cervix are these: there is a gland lying about one inch and a half or so away from the cervix on each side in the loose connective tissue of the broad ligament. It is not always present, but it is in many cases, and, when it is present, that is one of the glands affected in cancer of the cervix. One can recognise it at operations. The other glands which are affected in cancer of the cervix are the iliac glands. These are generally three in number, and they lie just about the bifurcation of the common iliac artery. One is generally rather towards the external iliac; the other two lie more deeply in the pelvis. These glands may be affected in advanced cases. It should be remembered that these glands are not by any means universally affected in cancer of the cervix, even in advanced cases. Probably in only about one third of the cases are the glands secondarily involved. That is an important point in connection with operations. And there is still one other point in connection with glands which I may mention, while talking of them, and that is that they may be considerably enlarged, and often are, and yet not be infiltrated with cancer. Several times I have removed an enlarged gland in the course of an abdominal hysterectomy for carcinoma and expected to find it carcinomatous; but subsequent microscopical examination showed there was no carcinoma in it; the enlargement was simply due to inflammation. There is an interesting point in that connection as to why the glands in cases of cancer of the cervix are involved at a com-

paratively late period, or not at all, as compared with cases of cancer of the breast, in which the glands are involved comparatively early, and I think the explanation which is put forward by some American writers is the true one, namely, that the cancer-cells in cancer of the breast are smaller, and therefore are able to get into the small lymphatic vessels readily, whereas in the case of carcinoma of the cervix the cells are large, and for some time at all events they are unable to get into the small lymphatic vessels in the neighbourhood. It is not until the disease is more advanced and some large lymphatic channel is invaded that infection of the glands can take place. That seems to me to be a reasonable explanation.

Cancer of the Body of the Uterus.

Now a word or two about carcinoma of the body of the uterus, in order to clear the ground. That is a much rarer disease than cancer of the cervix, and it affects an entirely different class of patient. In fact, the ætiology of carcinoma of the cervix is much more like the ætiology of fibroid tumours of the uterus—that is to say, it occurs more particularly in patients who have either had no children, or perhaps have had one child some years ago. There is a very large percentage of sterile women in a series of cases of carcinoma of the body of the uterus. With regard to age, that again is in some respects in contrast to what we find in cancer of the cervix. Carcinoma of the body of the uterus is pre-eminently a disease of advanced life; the majority of cases occur between the ages of fifty and sixty, or you might say forty-four to sixty. An age-period of that extent would comprise the large majority of any series of cases of carcinoma of the body of the uterus, and most of the cases would be between fifty and sixty years of age.

With regard to the actual symptoms in cancer of the body of the uterus, they are very similar to those of cancer of the cervix. Probably in the first instance there is some bleeding other than natural menstrual bleeding; that is the first thing to direct attention to it. But with regard to pain, which you also get in carcinoma of the body of the uterus, the pain comes on, when it does occur, very much earlier; it is a relatively early symptom in carcinoma of the body, and it is often very severe.

With regard to the diagnosis of carcinoma of the body of the uterus, you find on examination the vaginal portion of the cervix—at all events that is all the cervix you can get at—normal. There is a patient who has some bleeding, who may or may not have some severe hypogastric pain in the neighbourhood of the uterus, and when you examine her you find the cervix normal. If you have a somewhat advanced case, one which has been in progress some time, you find bimanually there is an enlargement of the body of the uterus. And that enlargement is more particularly striking because these cases generally occur at an advanced age, that is to say, when the menopause ought to have occurred, and consequently at a time when the body of the uterus, so far from being larger than normal, ought to be very much smaller because of the senile atrophy which normally occurs after the menopause. In a very early case, such as the one from which this specimen I show you was removed, you find that the body of the uterus is not very conspicuously enlarged; indeed, it may not be enlarged at all. But in many other cases where the disease has been for some time in progress you may find there is a considerable enlargement. Here is another specimen in which the enlargement is well marked.

As to diagnosis, the right course is to dilate the cervix, preferably in the first instance with a tent, and then subsequently with Hegar's dilators. Then either pass your finger or a curette into the body of the uterus. In many cases the tissue of the cervix is rather fragile in elderly women, at all events it is rather thin, and you may occasionally have some difficulty in dilating the cervix sufficiently to get your finger into the body of the uterus. It is not always absolutely necessary to dilate up to such a high degree. In order to get your finger into the body of the uterus you must dilate the cervix up to a No. 19 Hegar. There are some cases in which, if you persist in dilating up to that extent, you will be very likely to tear the cervix. Where you think there is some risk in going on with the dilatation you will probably get all the information necessary by using a blunt curette. This can be passed through a cervix which would admit an ordinary lead pencil; you then gently curette the endometrium. In the ordinary form

of carcinoma of the body you find there is an extremely brittle, soft, whitish-yellow growth, several fragments of which will come away. To those who have had experience of these cases such material is pathognomonic of cancer; though it is always well to examine the material removed under the microscope for confirmatory purposes.

Now a word as to the extension of the disease in the case of cancer of the body of the uterus. Cancer of the body of the uterus remains limited to the uterus for a very much longer time than does cancer of the cervix, and is a much more chronic disease. Cancer of the cervix is frequently a very acute process, tending to spread rapidly and involve the surrounding tissues quickly, and quite early. That is why so many cases come to us only when they are far advanced, often too far advanced for any operative treatment to be of avail for them. To illustrate the chronicity of carcinoma of the body of the uterus, I remember a case of it which was sent to me by a practitioner some years ago. I recommended the patient to have the uterus removed. She would not have it done, because she was afraid of operation, and accordingly went back to her home in South Wales. Five years afterwards the same practitioner was writing to me about another case and said: "You will be interested to know that Mrs. — has only just died." The cancer was well marked when I saw her, yet its progress had been so slow that it was not until five years afterwards that she died of it. If in her case the cancer had been in the cervix, she would probably have been dead in fifteen months. So remember that cancer is a more chronic condition when it occurs in the body of the uterus, and the prognosis in cases of it where hysterectomy is performed is much more favourable. The glands which are affected in cases of carcinoma of the body of the uterus are the lumbar glands, lying in front of the spinal column at the level of the lower end of the kidney, and at certain advanced stages of carcinoma of the body when the case has become inoperable glands in the groin may also be affected. It is said that the lymphatic vessels running along the round ligament into the groin are involved, and in that way the cancer spreads to the inguinal glands. But it is a very late complication.

The Operative Treatment of Cancer of the Uterus.

Now let us come to the operative treatment more particularly. It is very interesting to look over the facts showing the gradual evolution of the present position of affairs in this respect. The extent of the operation, so to speak, has gradually increased as knowledge of the various directions in which the disease tends to spread has been acquired, and as the technique of operative work generally has improved. In the early days—I am talking of thirty or thirty-five years ago—a patient with cancer of the cervix, if it was a reasonably early case, would probably have it scraped, perhaps it might be cauterised, and, if there was a projecting mass which seemed to lend itself to removal, that portion would possibly be cut off. Perhaps the wire of an écraseur would be put round it and the vaginal portion of the cervix amputated in that way. I remember very well, in a case twenty three years ago, putting the wire of the écraseur round a cauliflower growth in the vagina as big as my fist, tightening the wire, and cutting the portion off. I was very much concerned afterwards to find that included in the specimen was a definite piece of Douglas's pouch. The patient made a good recovery. But you see that operations of that kind merely amounted to removal of the projecting growth, or at most of the vaginal portion of the cervix, and were therefore of no real value because they were not likely to be followed by any prolonged improvement. The next advance from that position of things was when Schroeder, about the year 1875, advised the high amputation of the cervix. You will remember that the part of the cervix which you see by the speculum is only about one third of the whole cervix; there is a good deal above the vaginal reflection. He advised an operation to remove the whole of the cervix; and that constituted a very valuable step forward. Even now in vaginal hysterectomy the early stages of the operation are very similar to those required for removing the whole of the cervix. In order to remove the whole of the cervix at the level of the internal os you incise the vaginal cervix all round, and dissect away the bladder for half to three quarters of an inch, to the level of the internal os, that is to say up to the vesico-uterine pouch. This is also one of the steps in performing vaginal

hysterectomy. Not very long afterwards I began to be interested in this subject, and began to do the high amputation of the cervix. I have some specimens here, which have been kept all these years, showing removal of the cervix by what was practically Schroeder's operation. And I may say that that operation was, in a small proportion of cases, a sufficient operation, and no doubt still remains a sufficient operation, if you can be quite sure that the case in question is a favourable one. Of course we cannot be sure. In those days one performed the high amputation of the cervix as a routine operation, and it was sometimes sufficient to cure the patient, as shown very distinctly by this particular specimen. It is a cervix removed by high amputation for squamous-celled carcinoma on March 17th, 1887. This patient, fortunately, I have been able to follow, and to my certain knowledge she was perfectly well twenty years after the operation. One hesitates very much to speak of cure in relation to cancer, but I think twenty years without return of the disease sufficiently approximates to a permanent cure to satisfy most people. In a small proportion of cases of a favourable kind that operation was sufficient, and therefore it was a great advance on previous ones. But you can never be quite certain that the case on which you performed it was one which was going to have such a history. As a matter of fact, the majority of cases did not have a history like that; the majority were unfavourable. The next step was that by Freund, in 1878, who boldly determined to do abdominal hysterectomy for cancer of the cervix, and that was a great advance on anything which had been done before. He removed the uterus from above, that is to say he opened the abdomen, tied off the broad ligaments, dissected down the bladder, cut away the uterus and cervix from the vagina, and then drew his ligatures down into the vagina. Although this undoubtedly was an advance on previous work, the mortality from his operation was very heavy, and it rather discouraged people from following it extensively. About the same time, of course, vaginal hysterectomy began to be done. Pawlik, of Prague, in 1888 began to perform vaginal hysterectomy, and he began to do it with the assistance of bougies passed into the ureters in order to define their position. Looking at the cervix from the front, one of the great difficulties one has to deal with in all these operations which I have so far referred to—high amputation of the cervix, vaginal hysterectomy, and simple abdominal hysterectomy—one of the difficulties which you cannot overcome is that close on each side of the cervix there is the ureter. I have already said that one of the favourite directions for cancer of the cervix to spread is into the connective tissue at the sides of the cervix, and consequently into the immediate neighbourhood of the ureter. Looking at this specimen removed by vaginal hysterectomy you see that, in order to avoid the ureter, you have to divide the attachments of the cervix in this very small space which I indicate by a drawing; it is only one centimetre or one centimetre and a half in extent. You divide the uterus from its attachments and tie the attachments besides; but you must not tie the ureter. When you consider how the parametric tissue is affected, how early and how extensively, you will see that in very many cases the position of the ureter, so close to the cervix, prevents you getting a sufficiently wide separation to make the operation of any use. That is always a difficulty in vaginal hysterectomy, as well as in high amputation of the cervix; there is only a very narrow space in which to make your separation, and it must limit the usefulness of either operation to a very small proportion of cases. The same is true of abdominal hysterectomy of a simple type, such as Freund practised—abdominal hysterectomy without dissecting out the ureters. Many operators in the course of the next few years laid great stress on catheterising the ureters, because in many cases the ureters had been cut, or tied. Of course, if the ureters on both sides are tied the patient is doomed, and if only one ureter is tied the prognosis is bad. If the ureter is cut there is a ureteral fistula, which is very distressing, even if it is not dangerous; and often it may lead to an infective process spreading up the ureter to the kidney; there may be pyelonephritis, and the condition leads to the death of the patient. So many operators, in order to avoid the ureters as far as possible, catheterised them first, passed bougies into the ureters, and left them there as guides in vaginal and in abdominal hysterectomy. At the present time we have gone further than that. We have found that we can, without very much difficulty, and with a little

practice, dissect out the ureters quite satisfactorily without passing bougies in at all. And that undoubtedly is of very great importance. It is a difficult thing to pass bougies into the ureters; there is a possibility of infecting them, and there are several accidents which have occurred in the course of the operation, such as the breaking of a bougie in the ureter, when sometimes it has been found impossible to get it out. Cases of that sort are recorded which terminated fatally. Passing bougies into the ureters takes a considerable time, and therefore prolongs the operation, so that this procedure was very undesirable if the operation could be done without that. And Wertheim and others have shown that it can be done quite well without it. Mackenrodt, in 1894, went a step further, and suggested the removal of a good deal more parametric tissue here. As a rule you can get plenty of space above the growth in the upward direction, and a fair amount below, but not much space laterally, except by first dissecting up the ureters. And Ries, in 1895, devised another method of removing the uterus, laying great stress on removing the glands. About the same date Clark, an American operator, devised another method of removing the uterus with a considerable portion of parametric tissue, but he still used bougies in the ureters; that is to say, he dissected out the ureters by the aid of a bougie. The uterine arteries were tied outside the ureters. In his operation of abdominal hysterectomy the vagina was opened from above, and he finished the operation with a gauze drain through the vagina. He did not remove the glands. Rumpf went a little further, and devised a rather ingenious operation. He opened the abdomen, and dissected out the ureters, freed the uterus, except from its vaginal attachment—that is to say he freed the broad ligaments—and dissected down the bladder, and freed behind the rectum, and had the uterus simply attached by the vagina. And then he pushed the uterus down as much as he could towards the vagina, closing the peritoneal flaps over the uterus, and then put the patient into the lithotomy position, and incised the vaginal fornices from below, and so removed the uterus. That was a very ingenious operation, but it was rather complicated, and rather long, and I think that Wertheim's method of removing the uterus, as now practised, is a much better one; at present it seems to be an improvement upon all other methods, and it would appear very difficult to improve upon it.

"Wertheim's Hysterectomy."

We have a few specimens here which have been removed by Wertheim's hysterectomy, and if you compare them with some of those which have been removed by simple vaginal hysterectomy, you will see a considerable contrast in regard to the amount of parametric tissue removed. A great deal more connective tissue at the sides of the cervix, where infiltration is so common, is removed by Wertheim's method. With regard to Wertheim's hysterectomy, we have first of all to consider the indications for the operation, and the contra-indications. There is no doubt that the operability of cases of cancer of the cervix has been very much increased by the introduction of Wertheim's operation. Formerly, if there was any evidence that the disease had spread outside the uterus, that is to say, either into the connective tissue round the cervix, or at all extensively to the vagina, or still more if it spread to the lymphatic glands, the case was absolutely inoperable; nothing could be done. Vaginal hysterectomy in such cases is no good; you cannot remove the whole of the disease, or all the infiltrated tissue, and you cannot remove the glands, consequently the operation is not worth doing. Therefore Wertheim's hysterectomy, which enables us to remove a good deal more tissue than would be possible by vaginal hysterectomy, and also to remove infiltrated glands, has increased very much the operability of cases of this disease. Even now, however, we find cases which are too far advanced for any operation, even Wertheim's.

I divide cases of cancer of the cervix into three groups for clinical purposes. In the first group are the cases which are obviously early, in which the disease is quite limited to the cervix, the uterus is freely movable, and there is no evidence of extension. Such a case as that from which this specimen was removed comes into this group. Unfortunately those early cases are quite the exception. In the second group I place the cases where the disease is so extensive that directly you make an examination you at once conclude that the case cannot be dealt with by any operation, where perhaps the whole pelvic roof is converted into a

hard mass of cancer, or the whole of the pelvis filled with cancer, and the cancer perhaps extends down nearly to the vaginal orifice. Those cases, as I have said, are inoperable by any method. I do not think that, clinically, we see a very large number of cases in this group. Both the groups I have given you comprise the minority of cases which seek advice. That leaves us, as a third group, the intermediate cases. Most of the cases which we come across clinically will be found to belong to the third group. There is cancer of the cervix, more or less advanced; there is perhaps some extension to the vagina, more or less limited in kind; there is extension perhaps into the parametric tissue; thickening of one or other broad ligament; and possibly of the utero-sacral ligaments, and you may possibly feel the iliac glands enlarged. In cases of this kind, owing to the introduction of Wertheim's hysterectomy, we are prepared to operate at the present time, and in operating on such you must, I think, begin the operation, that is for cases in the third group, as an exploratory laparotomy. You cannot tell for certain until you are engaged in the process of doing the operation whether it is possible to remove the whole of the infiltrated tissue or not. In some cases in my own experience one has opened the abdomen and found, after a longer or shorter procedure, that it would be impossible, without killing the patient on the table, to remove the whole of the diseased parts. In some cases one has found glands extending nearly up to the diaphragm, and conditions of that kind, and such extensive deposits in the pelvis, perhaps, that without wounding one of the great iliac vessels, or taking away a piece of one of them, it would be impossible to remove the whole of the disease. I remember a case I saw in private a year ago where infected glands on the iliac vessels were quite irremovable. It was not an early case; as far as the uterus was concerned one could have dealt with it, but one found that there were enlarged glands on the left iliac vessels, and the question which arose was, could those glands be removed. I had done a good deal of the operation, stripped the bladder down, tied off the broad ligaments, and dissected out the right ureter. In dissecting out the left ureter I removed one of the glands which was breaking down, but other glands were fixed on to the large iliac vessels. The cancer had spread through the capsule of the gland, and involved the wall of the internal iliac artery and the iliac vein, and unless one could have removed a portion of these vessels it would have been no use to try to get the glands away; almost certainly one would have torn the vessels in the attempt. That, therefore, illustrates the kind of case where you can only decide in the course of the operation whether the procedure is feasible or not. I have done thirty completed Wertheim's hysterectomies at the present time, and there are besides seven in which I have been unable to remove the whole of the disease. So you must begin the operation as an exploratory laparotomy. There are certain special advantages in Wertheim's operation which are not found in the other operations. There are, as you will have seen, several sources of danger in any operation for cancer of the uterus. There is the risk of infection because the growth is generally in a very septic condition. There is also the risk of implantation of the cancer-cells on the raw surfaces, which are opened up in the course of the operation. Wertheim's method, if it can be carried out in its entirety, has the advantage that it enables one to shut off the septic and cancerous area in a sort of pocket formed by the vagina. I will give you a short description of the operation: The patient is first placed in the Trendelenberg posture. Then the abdomen is opened, and the round ligaments and the upper part of the broad ligaments are tied off and divided. Then the peritoneum is incised anteriorly just above its reflection on the bladder, and the bladder is stripped down as low as possible below the cervix, so as to produce a definite piece of vagina which is free from bladder tissue. One inch or more it may be, but the amount varies. You have now to dissect out the ureters. That is not so difficult with a little practice as it would seem. It certainly can be done well without passing bougies. You have to proceed cautiously, because it is easy to cut the ureters. You must dissect the ureters free from the pelvic brim to the bladder. In dissecting out the ureter you must be careful not to strip it too naked of its vascular attachments, otherwise there is a risk of sloughing of the ureter afterwards. On the other hand, you must have it fairly free, and it must be free enough to admit of being pulled aside when you are in the neighbourhood of the side of the cervix. You preserve as much of its attachments as you can

consistently with defining the ureter distinctly. Before dissecting out the anterior portion of each ureter you search for the uterine artery outside the ureter, and tie and divide it on each side. You now have the ureters free. Next you incise the peritoneum posteriorly at about the spot where it passes on to the vagina and strip that down, and at the same time strip back the rectum from the vagina. A very important part of Wertheim's method, as I have seen him do it in his own theatre, is the step I am about to mention. I went over to Vienna last year on purpose to see him operate by this method, and he kindly kept some cases for me to see. I saw him do the operation on three patients. One important step which he practised in the operation, and which I think many operators over here are not quite familiar with, comes in at the stage to which I have carried my description above. The uterus is free so far, the upper part of the broad ligament is free, the bladder is separated down, the vagina is exposed, and the rectum separated from the vagina. Wertheim now holds the uterus up as much as he can; you will find there are then several fibrous bands of connective tissue put on the stretch, particularly at the sides, in the region of the utero-sacral ligaments, and towards the cervix and vagina. An important step in Wertheim's operation as practised by himself is that these fibrous bands of connective tissue are clamped by means of large clamps, eighteen inches long; they are heavy and rather clumsy looking, and he puts on some ten or twelve of them altogether. He clamps a band, and then cuts it; clamps another and cuts it, and so on until he has the uterus attached by the vagina only. That is the important point I want to bring out. Those connective-tissue bands keep down the uterus and cervix in the depths of the pelvis, and it is not until they have been thoroughly divided, that the uterus is sufficiently freed for the vaginal clamps to be easily applied. Those who find difficulty in applying Wertheim's vaginal clamps at the end of the operation, just before cutting the uterus free from the vagina, do not free the uterus sufficiently from these connective-tissue attachments. If you divide these attachments sufficiently you are able to draw the uterus up, as it is attached by the vagina alone, and can apply the clamps to the vagina almost, in many cases, on a level with the abdominal wound. The cancerous tissue and any associated septic discharge are thus confined in the portion of the vagina above the clamp. The vagina is then cut across below the clamps, and the whole of the specimen is then lifted away with the clamps still attached. In the three cases I saw operated on by Wertheim, he applied the vaginal clamps almost on a level with the abdominal wall, instead of having to go down into the depths, so to speak, to clamp the vagina. That shows how freely he separates the deep connective-tissue attachments.

The mortality after Wertheim's operation is rather a formidable matter. He has arranged his cases in series of thirty, and in June, 1908, had done the operation more than five hundred times. In his first series of thirty he said his mortality was about 40 per cent. In his last series of thirty it had sunk to between 7 per cent. and 8 per cent. I lost four out of my first ten cases, but only two out of my next twenty. Considering the class of cases operated on—all but one too far advanced for vaginal hysterectomy to be worth doing—I think the results have been very satisfactory. There is another thing to be thought of in relation to mortality, namely that the risk varies very much according to the degree of advancement of the disease. If an operator does this operation on very early cases, such as the case from which this specimen was removed, there is no reason why there should be any mortality at all. The mortality rises rapidly in proportion as you endeavour to deal with more advanced cases: the more advanced the case the more difficult and dangerous the operation. So, in a sense, favourable statistics may easily be too favourable, and may indicate that only early cases are being dealt with; whereas one of the chief merits of Wertheim's operation is that it enables us to deal, with a good prospect of success, with cases which are relatively advanced—cases too far advanced to be operated on by any other method.

Now a word or two about the contra-indications for the operation. Of course, cases of cancer of the cervix which you see may be in the second group I mentioned: they may be too far advanced even for Wertheim's operation. But, quite apart from that, there are other contra-indications. The operation is a long one, even in the hands of Wertheim himself, although he is a rapid operator. It is inevitably a long operation; so that a patient

who is not fit to stand a prolonged operation should not have this operation performed on her. In regard to the next point, I am of course speaking provisionally, but if a patient is over sixty years of age I consider she is generally not suitable for Wertheim's operation; she is unlikely to survive the operation if it is attempted upon her. I have here a specimen of cancer of the cervix removed recently which I call your attention to as illustrating the extension of cancer of the cervix into the body of the uterus. It is not an early case, although on examination prior to operation it seemed to be so. That uterus was removed by vaginal hysterectomy rather than by Wertheim's operation, because the patient was a woman æt. 62 years, and I did not think she would stand the longer operation. With the exceptions mentioned I think Wertheim's operation ought to be the general operation for cancer of the cervix, and also for cancer of the body of the uterus. It is pre-eminently the operation for cancer of the cervix, but it has some advantages in cases of cancer of the body. Here is a specimen of very extensive cancer of the body complicated with fibroids which was removed by Wertheim's hysterectomy. The growth which you see here is exceedingly friable, and remember that in the operation you are holding the uterus up, squeezing it and manipulating it, and what happens invariably in ordinary pan-hysterectomy for cancer of the body of the uterus is, that some of this growth, which is often also in an infective and fœtid condition, is squeezed out of the os uteri into the upper part of the vagina; therefore, when you cut across the vagina you find your fingers in a *débris* of cancerous growth, and also sometimes of septic matter. This complication is altogether avoided by Wertheim's operation. It is an operation which may be very well applied to cases of cancer of the body of the uterus as well as to those of cancer of the cervix. In the case of cancer of the body it is a relatively easier operation, because as a rule cancer of the body has not, when you see the case, spread into the connective tissue at the sides of the cervix, and consequently there is not that excessive difficulty in getting the uterus up, and clamping the vagina at a convenient level. The advantage of clamping is that you confine all the septic and cancerous material in the pocket above the clamps. Before you cut across the vagina you mop it out with sterilised gauze. Having cut it across, the clamps prevent any of this material fouling the wound. So that for cases of cancer of the body of the uterus, as well as for those of cancer of the cervix, I consider that at the present time Wertheim's operation is by far the best.

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SOME DISORDERS OF THE CEREBRAL CIRCULATION AND THEIR CLINICAL MANIFESTATIONS.*

By ALFRED E. RUSSELL, M.D., F.R.C.P.,
Physician to Out-patients, St. Thomas's Hospital.

LECTURE III.

(*Concluded from p.* 397.)

On Diminution in the Blood-Flow through the Brain as the Result of Increased Intra-Cranial Tension.

The experimental results following increased intra-cranial tension have been studied by Harvey Cushing.† He increased intra-cranial tension in dogs by suitable means, and he showed that, if the intra-cranial pressure be rapidly increased, "Kussmaul-Tenner spasms, evacuation of bladder and rectum, practical cessation of respiration, and pronounced vagus effect upon the heart, often with a complete standstill, lasting from ten to twenty seconds, may develop. Then follows a release from this extreme vagus inhibition, and the vaso-motor centre exerts its influence." With a slower increase of the intra-cranial pressure a different series of events occurred. The pressure against the brain could be increased to the point of its equalling the blood-pressure before any symptoms referable to the centres in the medulla were called forth. Direct examination of the cortex through a circular disc of glass fitting tightly into a second trephine hole showed, at this period of equalisation of blood-pressure and intra-cranial tension, an abrupt blanching of the exposed convolutions. The pulsating arteries could be seen against the blanched background and the dark blue veins in the sulci remained filled with blood, but presumably little, if any, circulation passed between them. The usual consequence was not death but a stimulation of the vaso-motor centre, which occasioned a rise in blood-pressure sufficient to overcome the high intra-cranial tension; the cerebral circulation was re-established, and the rosy colour could be seen through the glass window in the trephine hole to return again to the blanched

* The 'Goulstonian Lectures,' delivered before the Royal College of Physicians.

† "Some Experimental and Clinical Observations concerning States of Increased Intra-cranial Tension," 'Amer. Journ. of the Med. Sciences,' 1902, cxxiv, p. 375.

convolution. With further increase in intra-cranial tension the blood-pressure rose *pari passu*, and always to a point exceeding the intra-cranial tension. This process could be repeated until the arterial pressure was forced to two or three times its normal level, sometimes to as much as 250 mm. Hg., without evidence of vaso-motor failure. In face of these experiments, Cushing's conclusion that increased intra-cranial tension occasions a rise of blood-pressure, which tends to find a level slightly above that of the pressure exerted against the medulla, seems absolutely justified. By this mechanism the vital centres in the medulla and the life of the brain and entire animal are protected.

Clinically it is well established that many of the symptoms of cerebral tumour, hydrocephalus, cerebral hæmorrhage, etc., are dependent upon an increase of the intra-cranial vision. Among such symptoms may be mentioned headache, vomiting, coma, convulsions, choked disc, etc. Extraordinary relief to these symptoms is attained after the pressure is relieved by surgical intervention. An admirable series of cases has been recorded by Harvey Cushing.*

In another paper Cushing† gives the records of five cases of intra-cranial hæmorrhage, four traumatic and one apoplectic. These illustrate, from the clinical standpoint, the facts ascertained by him experimentally.

In one case of apoplectic cerebral hæmorrhage the blood-pressure before operation registered 300 mm. Hg., whilst after trephining and the evacuation of blood it began to fall at once, and in twenty minutes had reached the normal.

The clinical evidence as obtained, therefore, from cases of cerebral tumour, cerebral hæmorrhage, etc., is in complete accord with the conclusions arrived at experimentally by Harvey Cushing. To recapitulate, it is clear that a rise in intra-cranial tension produced by the introduction of any foreign element, such as a tumour mass, blood, etc., must tend to diminish the blood-flow through the brain. As the tension increases, a point would be reached at which the intra-cranial tension equals that of the general blood-pressure. The cerebral circulation would therefore cease, were it not that by a compensatory process the general blood-pressure rises to a point above that of the intra-cranial pressure, and thereby maintains the flow of blood through the brain. But with a great increase of intra-cranial tension certain general effects are produced, apart from focal symptoms, dependent upon the position of the lesion. Headache, for instance, is common, and is probably attributable to tension of dura mater and tentorial structures.

Optic neuritis is to be attributed, in the main, to a passive venous congestion of the retinal veins, and subsides or improves on relief of intra-cranial tension, sometimes with extraordinary rapidity.

Finally, coma is almost invariable in the last stages of cerebral tumour, and in large cerebral hæmorrhages. Convulsions are also frequent in these conditions. Both are remarkably improved by methods capable of lowering the cerebral pressure, such as trephining or lumbar puncture. And it is to be noted that, by lowering the intra-cranial tension, a free access of blood to the brain is facilitated.

Uræmia.

Uræmic convulsions may be absolutely indistinguishable from those of idiopathic epilepsy, and if it can be shown that there is evidence of a condition of cerebral anæmia in uræmia, support would be lent to the similar theory as applied to epilepsy. In a paper read before the West London Medico-Chirurgical Society I brought forward evidence to show that the cerebral manifestations of uræmia are due to cerebral anæmia produced by an increase of intra-cranial tension, resulting in all probability from cerebral œdema.*

In cerebral uræmia we frequently see a symptom-complex almost identical with that of cerebral compression, viz. headache, vomiting, drowsiness, coma, convulsions, optic neuritis, etc. This symptom-complex is, at any rate in great measure, dependent upon increased intra-cranial tension; for many cases are now on record in which extraordinary relief has followed lumbar puncture, a procedure which, by means of allowing some of

* "The Establishment of Cerebral Hernia as a Decompressive Measure for Inaccessible Brain Tumours," 'Surgery, Gynæcology, and Obstetrics,' 1905, i, pp. 297–314.

† "The Blood-pressure Reaction of Acute Cerebral Compression illustrated by Cases of Intra-cranial Hæmorrhage," 'Amer. Journ. of the Med. Sciences,' 1903, cxxv, p. 1017.

* "Uræmia," 'West London Medical Journal,' 1907, xii, p. 9.

the fluid to escape, diminishes the pressure within the cerebro-spinal space. Numerous cases of uræmia were quoted from the literature in which marked relief had followed on the lowering of intra-cranial tension by means of removal of cerebro-spinal fluid by lumbar puncture. I will only quote here Willson's cases as a type. In two papers he records ten cases.* Of the ten cases, six had convulsive movements, general in five and unilateral in one. In every case the convulsions terminated on the withdrawal of the cerebro-spinal fluid, and in only one did they return within several weeks of the operation. His best results were obtained in those cases in which the fluid spurted from the cannula, *i. e.* in which the pressure was greatest. In the autopsies of fatal cases (three out of the ten) increased cerebro-spinal fluid, dilated ventricles, and œdema of the brain were found. A sufficient number of cases were quoted to show that marked relief may follow lumbar puncture in cases of uræmia. It is well known that uræmic convulsions and coma may disappear apart from such treatment, but the promptitude with which the improvement occurred was such as to leave no doubt in the minds of the observers that the relation was one of cause and effect. It is noteworthy also that in most of the cases the cerebro-spinal fluid did escape under considerable pressure.

The cerebro-spinal space is a practically closed-in cavity, with walls of considerable rigidity. This cavity is always full of fluid or semi-fluid substance, and to force more fluid into such a space would necessitate great pressure, were it not that by compression of blood-vessels the volume of blood contained in the cranium can be diminished. But after a certain point the peripheral blood-pressure rises, and further accumulation of fluid would meet with rapidly increasing resistance, and a small additional quantity would materially raise the cerebro-spinal pressure ; *vice versa*, the removal of a very small quantity could materially lower it.

But relief has not always attended the performance of lumbar puncture in uræmia, and this may be due to the fact that this operation can only relieve intra-cranial pressure by removal of the *free* cerebro-spinal fluid. If, however, the pressure is mainly produced by a cerebral œdema, then, unless a co-existent excess of free ventricular fluid was present, the removal of the little that would flow might not be sufficient to relieve the pressure materially.

The manifestations of uræmia here considered, which are so strikingly relieved by lumbar puncture, are, as has been pointed out, closely similar to the pressure symptoms produced in other conditions, such as cerebral tumour and cerebral hæmorrhage, and the fact that the cerebro-spinal fluid is often under considerable pressure in these cases of uræmia indicates that the underlying condition of increased intracranial tension must be responsible for the symptoms.

Harvey Cushing, indeed, makes this suggestion in the paper on the establishment of cerebral hernia above referred to: "I have come to believe that the same causes must underlie the choked disc of tumour and the so-called retinitis associated with renal disease. It seems not improbable that an increase of intra-cranial tension due to cerebral œdema may be responsible for the occasional retinal changes in Bright's disease, as well as for the headache and vomiting which may characterise it."

The correctness of Cushing's views, founded on a series of brilliant researches, both experimental and clinical, are still further supported by a recent account of a case of uræmia in which sub-temporal decompression was attended with must successful results.*

The patient was a woman, æt. 22 years, with œdema, headache, and vomiting. Both discs were swollen. Right 6 D., left 7 D. The discs were very œdematous, the physiological cup was filled in, and there were many retinal hæmorrhages. Vision failed rapidly. Later the retinæ were so swollen that it was impossible to locate the discs. The retinæ were covered with hæmorrhages and yellowish-white patches of exudation, and the arteries were invisible. Lumbar puncture gave no relief. Right subtemporal decompression was

* Willson, "The Pathogenesis of Uræmia and Eclampsia," 'Journ. of Amer. Med. Assoc.,' 1904, p. 1019; also "The Relief of Uræmic Hemiplegia and other Uræmic States by Lowering Intra-cranial Pressure," 'Transactions of College of Physicians of Philadelphia,' 1905, xxvii, p. 34.

* Harvey Cushing and James Bordley, jun., "Subtemporal Decompression in a Case of Chronic Nephritis with Uræmia, with Special Consideration of the Neuro-retinal Lesion," 'Amer. Journ. of Med. Sci.,' October, 1908

performed. The dural veins were considerably congested, the arteries markedly tortuous and sclerotic. The subdural space contained no free fluid. The arachnoid was *markedly distended with fluid*, which escaped after pricking the membrane in spaces where it bridged over the sulci. The brain itself appeared "soggy and wet." The headache subsided, stupor rapidly disappeared, and the patient's lethargic state was replaced by one of normal mental activity.

Eleven days later the swelling of the discs did not exceed 1 D., and the retinal tissue was much clearer, and still further improvement had occurred by the time she left hospital. She was admitted a month later, stuporous and with Cheyne-Stokes' breathing. Death was due to cerebral hæmorrhage, and the kidneys were small and granular.

The authors' conclusions were that the neuro-retinal and cerebral manifestations of uræmia are due to œdema of the brain.

Uræmic Coma.—The foregoing facts indicate that in uræmia a state of increased intra-cranial tension is present, and that relief of tension by lumbar puncture or decompression causes a marked alleviation of the symptoms. Traube's view that cerebral œdema (which would produce the rise in the intra-cranial tension) is the cause of anæmia is strongly supported by the above facts, and especially by the striking case of decompression.

The late Dr. Beevor also remarked when injecting brains of people dead from various causes, that "it was particularly observed that the cases, where the injection did not penetrate well were those suffering from granular nephritis or alcoholism, where there was much fluid in the subarachnoid space of the brain." *

Concurrently with the increase of intra-cranial tension the blood-pressure rises, and we see the slow, tense pulse so common in uræmia. This conservative rise of blood-pressure maintains the cerebral circulation. If the tension progressively rises the compensatory rise of blood-pressure cannot go on indefinitely, and a point may be reached beyond which no amount of vaso-constriction and cardiac augmentation can maintain an adequate cerebral circulation. If this point is reached gradually and the volume of blood passing through the brain be slowly diminished, we should expect a comatose condition to develop, the last stage of cerebral compression with gradual respiratory failure, the high-tension slow pulse of the early stage of compression changing into a soft, rapid pulse, with the developing vaso-motor failure. A concomitant toxic action on the brain is not denied; such may be present and aid in the production of the cerebral symptoms. But the anæmia alone should suffice to induce the coma.

Uræmic convulsions.—Under the severe strain imposed upon the heart in working against this conservative high blood-pressure it may fail rapidly in chronic nephritis. Should this occur, or should the vaso-motor centre fail rapidly, it is clear that the cerebral circulation must fail equally rapidly when the intra-cranial tension is pathologically high. Instead of headache and somnolence, gradually developing into coma, a more sudden unconsciousness would result, and convulsions would readily be produced.

According to Strumpell,* "the pulse is often very slow before the appearance of severe symptoms, sometimes 48 or 40, but it is almost always tense and hard. In chronic uræmia also a moderate slowness of the pulse is not infrequent. When uræmic convulsions appear, however, the pulse usually becomes small and very frequent, especially in cases that terminate unfavourably."

Willson's cases above recorded are of the greatest importance in this connection, especially as, in his six cases of uræmic convulsions, the convulsions terminated in every case on the withdrawal of the cerebro-spinal fluid; and it is to be noted that his best results were obtained in those cases in which the fluid spurted from the cannula, *i.e.* in which the pressure within the cerebro-spinal space was greatest. And this withdrawal of fluid, by lowering the cerebral pressure, would allow of an immediate return of blood to the brain.

In cases of acute uræmia in acute nephritis it is well known that an increase of blood-pressure is common, and the cardiac failure may be more readily induced owing to the more toxic character of some of the diseases associated with acute nephritis, the poisons of the acute infections, such

* C. E. Beevor, "On the Distribution of the Different Arteries Supplying the Human Brain," 'Royal Soc. Phil. Trans.,' 1908, series B, vol. cc, p. 15.

* Strumpell, 'Text-book of Medicine,' third American edition, p. 600.

as scarlet fever, materially affecting the heart muscle. The heart would thereby be unable to respond to the vaso-constriction above described, and the conservative rise of blood-pressure would fail more rapidly.

In conclusion, it is submitted that the pathology of the cerebral manifestations of uræmia is to be sought in a condition of œdema and increased intra-cranial tension with failure of the cerebral circulation produced in the manner suggested, a gradual failure producing coma, a rapid one, convulsions.

If this conclusion be correct, strong support is lent to the theory that the fits of idiopathic epilepsy are produced by sudden failures in the cerebral circulation, for it is notorious that the convulsions of uræmia and of idiopathic epilepsy may be absolutely indistinguishable, and it is extremely probable that the factor underlying conditions so remarkable and so identical should be one and the same.

The local palsies of uræmia.—In addition to the headache, convulsions and coma of uræmia local palsies may occur, such as hemiplegia, monoplegia, aphasia, amaurosis, etc. These are often only temporary and must therefore be due to some factor which may appear, last for a variable time, and then disappear. Two possible factors at once suggest themselves—arterial spasm and localised cerebral œdema. Both have been suggested as possible explanations of these local and transient symptoms of uræmia.

The question of cerebral vaso-motor spasm has been discussed in a previous lecture, and such spasm has been brought forward by various observers as a possible explanation of the transient paralyses of arterio-sclerosis. I think that some of these latter, especially those noted on awaking from sleep, may depend on a passing depression of the blood-pressure diminishing the blood-flow through a diseased and narrowed artery to a point below that essential for adequate nutrition of the related area of brain tissue.

Local œdema of the brain would be equally efficacious in arresting or diminishing the blood supply, and Cushing and Bordley noted in their case that "the arachnoid was markedly distended with fluid which escaped after pricking the membrane in spaces where it bridged over the sulci. The brain itself appeared soggy and wet."

Collateral evidence of the occurrence of localised cerebral œdema may be found in a case published by Professor Osler.

"The patient was a medical man æt. 29 years. At the age of twelve he had an attack of right hemiplegia and aphasia which lasted for a week or ten days. Within the year he had five or six further attacks of hemiplegia, each successive one less severe and not accompanied by aphasia, and from that date was subject to occasional attacks of numb, tingling sensation in the side. From the age of twenty-six he became subject to severe attacks of migraine. At twenty-eight he had a sudden attack of swelling and pain in the feet, and at the same time he began to suffer from soreness at the ends of the fingers. He had frequent attacks of angio-neurotic œdema of the upper lip and outbreaks of urticaria associated with severe darting pains in the legs. He had one attack of abdominal colic with pains in the calves of the legs and an outbreak of purpura and urticaria; later he suffered from hæmaturia and albuminuria. Professor Osler considered that the recurring attacks of hemiplegia were probably associated with changes in the brain of essentially the same nature as those which subsequently occurred in the lip and skin—in other words that an angio-neurotic œdema occurred in the brain substance, and it is difficult to see how this conclusion can be avoided.

I quote this case in detail because it does give support to the view that local œdema can occur in the brain and can give rise to local paralyses. Inasmuch as these paralyses are so frequently transient the direct evidence of the post-mortem table is not available.

Cushing and Bordley, as the result of their observations on their cases of cerebral decompression, came to the conclusion that the local and transient hemiplegias, aphasias, amauroses and Jacksonian fits of uræmia, were also due to œdema of the brain.

Status Epilepticus.

Morgan Hodskins and Arthur Morton* have reported a series of seven cases of status epilepticus treated by lumbar puncture. As they are of considerable importance I give them in some detail.

"Case 1.—March 26th, 1904: After forty fits (at intervals of about fifteen minutes) lumbar puncture was performed; 12 c.c. of fluid withdrawn, not under very high pressure. Convulsions ceased for over two hours, then recurred, thirty-five in the next two days, but not so severe. Then slow recovery.

* "Lumbar Puncture in Status Epilepticus," 'Boston Med. and Surg. Journ.,' 1905, clii, p. 700.

"CASE 2.—April 18th, 1904: Status epilepticus. One hundred grains of sodium bromide given hypodermically with no effect. Lumbar puncture after twenty-four severe fits, and 14 c.c. fluid withdrawn under increased pressure. Only one more fit in next twelve hours, then a few slight ones, easily controlled, followed by exhaustion, paralysis of pharynx and extremities. Slow recovery.

"CASE 3.—April 18th, 1904: Twenty-five fits. Lumbar puncture, and removal of 14 c.c. of fluid under slightly increased pressure. Five slight fits in next two and a half hours, then cessation of fits and quick recovery.

"CASE 4.—May 19th, 1904: Twenty-five fits. Lumbar puncture; withdrawal of 14 c.c., not under greatly increased pressure, until convulsions occurred, when it squirted out in a stream. No effect; seventy-five fits in twenty-four hours, and death on following day.

"CASE 5.—August 29th, 1904: Seventy-five to one hundred fits daily for past three days. Lumbar puncture and withdrawal of 15 c.c. under considerable pressure. Free from fits for three and a half hours, then a recurrence, the temperature rising to 109° F. before death.

"CASE 6.—Status epilepticus. September 12th, 1904: Status for thirty-six hours. Lumbar puncture; 15 c.c. of fluid withdrawn under increased pressure. Free from fits for eight hours; then return of fits. Rise of temperature to 107° F. Death.

"CASE 7.—Status epilepticus. October 12th, 1904: Twenty-five fits. Lumbar puncture; 20 c.c. of fluid withdrawn under increased pressure, followed by injection of 10 c.c. of sodium bromide solution (gr. xxx to the ounce). One fit occurred in the next fifteen hours. Slow recovery. The blood-pressure, which before the puncture measured 140 mm. of mercury, fell to 127 mm. afterwards."

In another case reported by R. C. Allen * lumbar puncture was performed at the end of prolonged status when death appeared imminent. The cerebro-spinal fluid spurted out under considerable pressure; three ounces were allowed to escape. The fits ceased and improvement was immediate. The pulse, which was barely perceptible, became stronger. Consciousness returned in twelve hours, the patient was torpid and lethargic for six days, and then became perfectly well.

It is noteworthy that in five out of the eight cases recovery ensued, and that in every case but one there was an immediate and marked improvement as the result of the lumbar puncture. Further, in seven of the cases the cerebro-spinal fluid was evidently under increased pressure, and in the only case in which the blood-pressure was estimated it fell from 140 mm. of mercury to 127 mm. as the result of the puncture. These facts suggest that the condition of status is similar to what is seen in uræmia, in which, as has been pointed out, there is an increase of the cerebro-spinal pressure. And this increased pressure would tend to produce an anæmia of the brain unless the blood-pressure rose to a point higher than that obtaining within the cranial cavity. The inference, therefore, that status epilepticus is due to anæmia of the brain brought about by increased intra-cranial tension does not appear unreasonable. It is possible that an unduly severe and prolonged fit in some way evokes œdema of the brain, and that the increased pressure resulting from this is responsible for the anæmia and the continuance of the fits.

Mott * has shown that "the essential changes in the brain in cases of status epilepticus are:—

"(1) Great venous congestion and stasis.

"(2) *Œdema of the brain* and marked distension of the perivascular lymphatics, flattening of the convolutions and naked-eye increased vascularity; but inasmuch as the brain is contained in a closed cavity, venous stasis and œdema must be associated with a corresponding *arterio-capillary anæmia.*"

It is interesting also to note that Mott finds that experimental ligature of arteries in animals leads not only to anæmia of the brain, but also to œdema. Continuing the above quotation:

"In the case of experimental ligation of arteries in animals the effect may be similar, but it is brought about by an entirely converse process; the œdema of the brain and venous stasis are here proportional to, and determined by, the diminution of arterial blood in the arterio-capillary systems. . . . Microscopical observations show that the whole brain is permeated by a canalicular lymph system containing cerebro-spinal fluid, the large processes of the neurons lying in lymph spaces which are continuous with the perivascular lymphatics. These perineuronal spaces were very obvious in some of the cases of experimental anæmia."

In this connection it is a striking fact that, in his description of the photo-micrographs accompanying his paper, Mott comments on the close similarity between the appearance of the brain-cells and perineuronal spaces in experimental anæmia of the brain (by ligature) and in status epilepticus.

These observations, both clinical and pathological, lead to the conclusion that the fundamental condition underlying the condition of status epilepticus is cerebral œdema and anæmia. It might be urged that, inasmuch as it is not probable that there is a great rise of cerebral pressure, the heart should be able to respond by

* 'Brit. Med. Journ.,' April 11th, 1908, p. 865.

* "Preliminary Communication upon the Changes in the Brain, Spinal Cord, Muscles, and other Organs, found in Persons Dying after Prolonged Epileptiform Convulsions," 'Archives of Neurology,' London, i, p. 499.

more powerful contractions which would maintain the cerebral circulation (*vide* Harvey Cushing's observations). It is interesting to note in this connection that the heart in cases of status epilepticus shows extreme fatty degeneration; thus Mott* has shown that "the œdema of the muscle substance of the heart is very striking upon microscopical examination; networks of capillaries are seen, small hæmorrhages are sometimes observed, and the fibres are separated from one another by a serous exudation. This of itself would embarrass the much over-worked organ; but the lymph around the muscle-fibres no longer constitutes a normal environment; it contains excess of carbonic acid, deficient oxygen, and toxic fatigue products, the result of excessive muscular activity and imperfect metabolism. The fibres, thus imperfectly nourished and oxygenated, are the seat of an imperfect metabolism which is manifested upon microscopical examination by a lustreless appearance, indistinctness of striation and accumulation of minute particles of fat in the substance of the fibres. . . . In seven cases of status epilepticus, and in a large number of cases of general paralysis dying after prolonged convulsive seizures, I have invariably found this fatty change in the heart and striated muscles."

The Epileptiform Seizures of General Paralysis.

Mott has shown that "œdema of the brain, owing to dilatation of the perivascular lymphatics, is a striking feature in general paralysis, and the water which can be extracted from the brain by placing it in a desiccator is larger in amount than in the normal brain. But venous congestion and œdema of the brain must be associated with arterial anæmia. . . . If all the arteries to a dog's brain be ligatured there is established an arterial anæmia, but the veins of the cortex will be found greatly congested, the perivascular lymphatics distended, and the motor cortex excitable, even hyper-excitable, to electric stimulation. This makes it probable that the epileptiform seizures of general paralysis are associated with and probably dependent upon venous congestions and stasis, arterial anæmia and increased excitability."

Conclusions.

In these lectures it has only been possible to touch upon certain aspects of a very large and difficult subject. It has been my purpose to endeavour to show that variations in the cerebral circulation, apart from gross lesions such as hæmorrhage, thrombosis, and embolism, exercise a very great influence in the production of nervous symptoms. Such variations in the cerebral circulation are often associated with equally marked variations in the peripheral circulation and in the action of the heart. It has been submitted that alterations in the circulation afford an adequate explanation, not only of the ordinary fainting fit, but also of the more prolonged attacks characterised by cardiac, vasor-motor and cerebral symptoms. I have urged that these cases, which in some respects are so closely allied to epilepsy, the suddenness of some faints and the conversions of faints into fits, afford strong evidence that the epileptic fit itself owes its origin to some disturbance of the circulation. Corroborative evidence is afforded by the accuracy with which the symptoms of the various stages of the epileptic fit are reproduced in cases of heart-block due to heart disease. Finally, evidence of the cessation of the heart's activity in epilepsy has been given. In the case of *petit mal* it has been suggested that two different factors may be concerned. In some cases the transient unconsciousness may be produced by a very transient cardiac failure; in others cerebral vaso-motor spasm may be concerned.

If these views are correct the pathology of epilepsy is carried only one stage further. The reason of these morbid cardio-vascular changes is yet to seek. A hereditary factor is obvious, and we must assume that there is an inherited instability of the sympathetic and cardio-vascular systems. The processes, both nervous and chemical, by which the cardio-vascular apparatus is governed are still far from clear; research in these directions may afford the clue to much that is at present obscure.

The serious symptoms produced by more prolonged cessation of the cerebral circulation have been considered.

Finally, the cerebral manifestations of uræmia have been discussed. It has been submitted that these are simply due to increased intra-cranial tension with resultant interference with the cerebral circulation. Evidence has been given to show that this change is amply sufficient to account for all the manifestations of uræmia. It does not negative the importance of abnormal metabolic changes, which may have great influence in the production of other uræmic symptoms.

If I have seemed to dwell too fully on cases collected from the literature it is because such cases contain evidence of the views I have put forward, and as they have not been published with such intention, the evidence may be taken as quite unbiassed. Owing to the inherent difficulties before mentioned, viz. the evanescent character of many of these vascular changes and the fact that when they have subsided no organic change is left behind, this cumulative clinical evidence yields the chief clue to the nature of the processes we have been studying, pending the discovery of the real pathological change on which they depend.

October 4th, 1909.

* Mott, *loc. cit.*, pp. 502, 503.

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